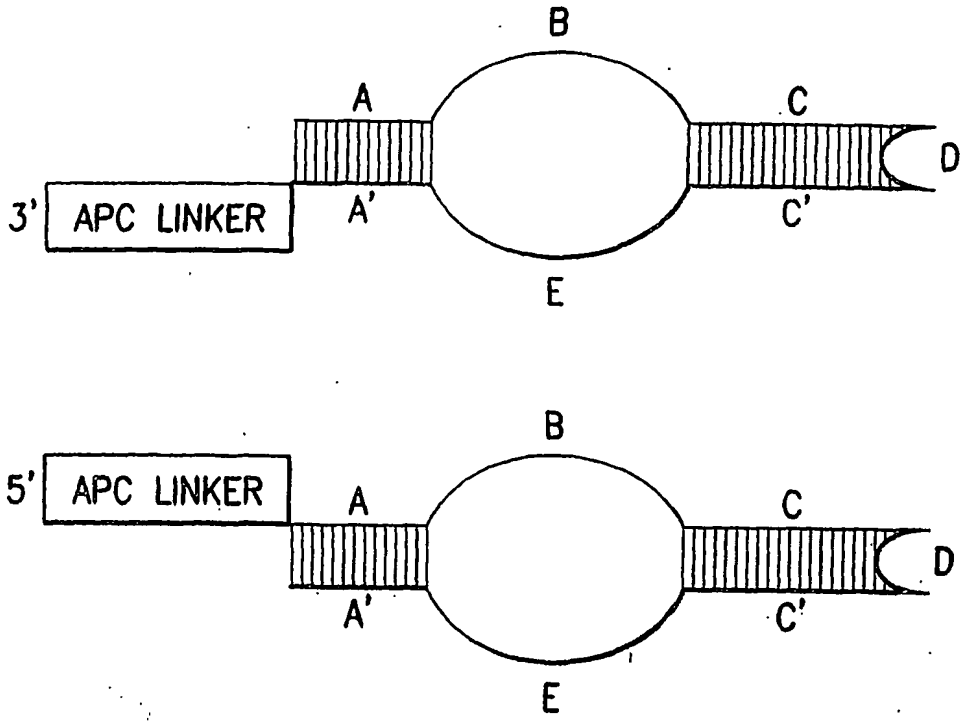


FIG.1

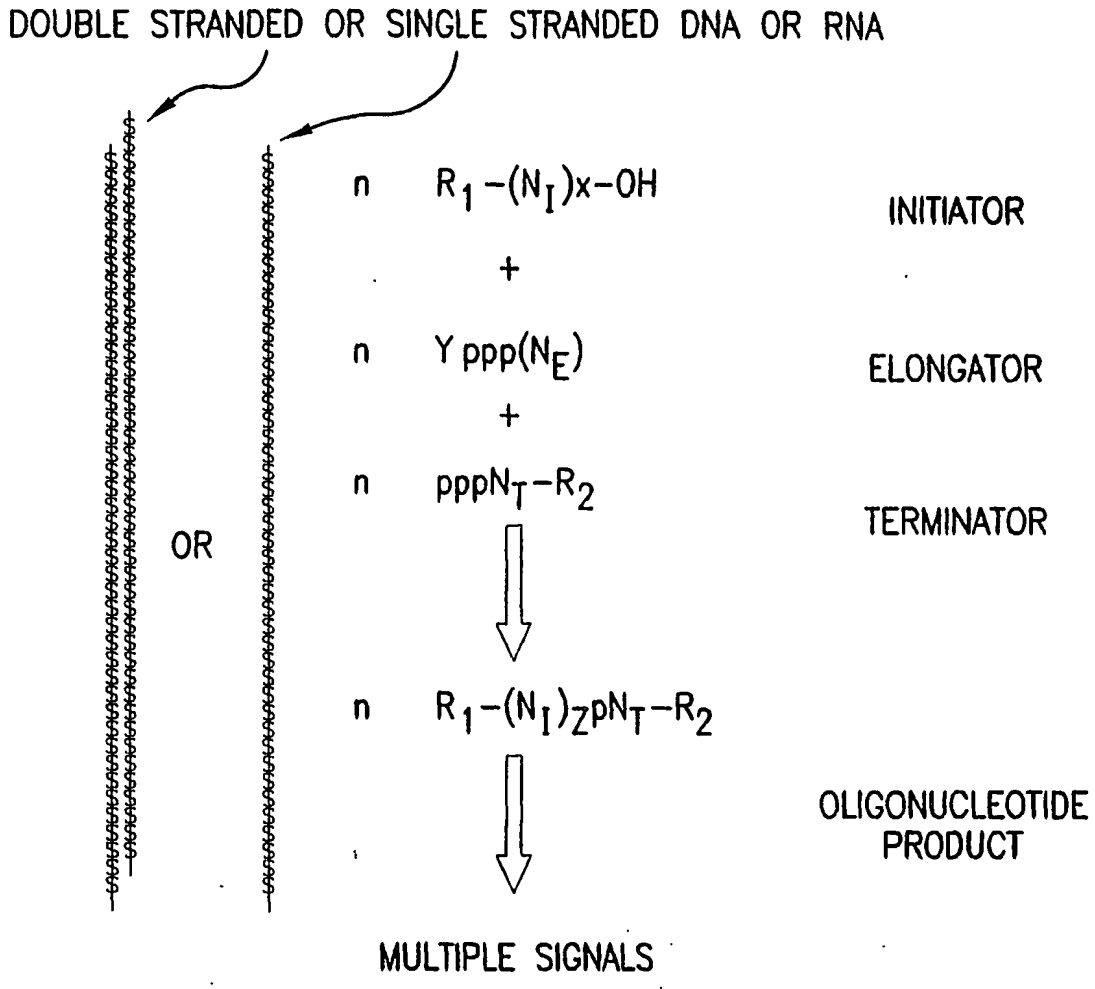
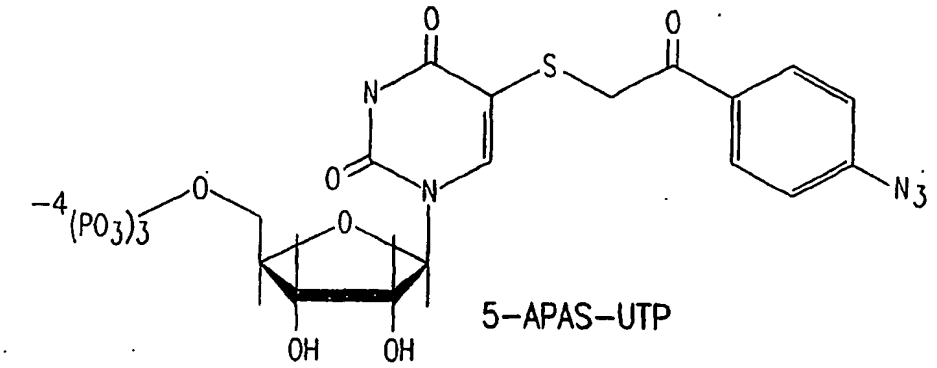
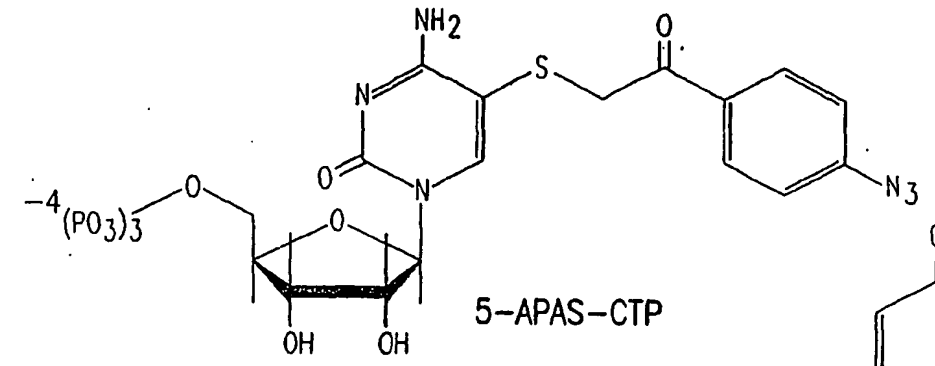
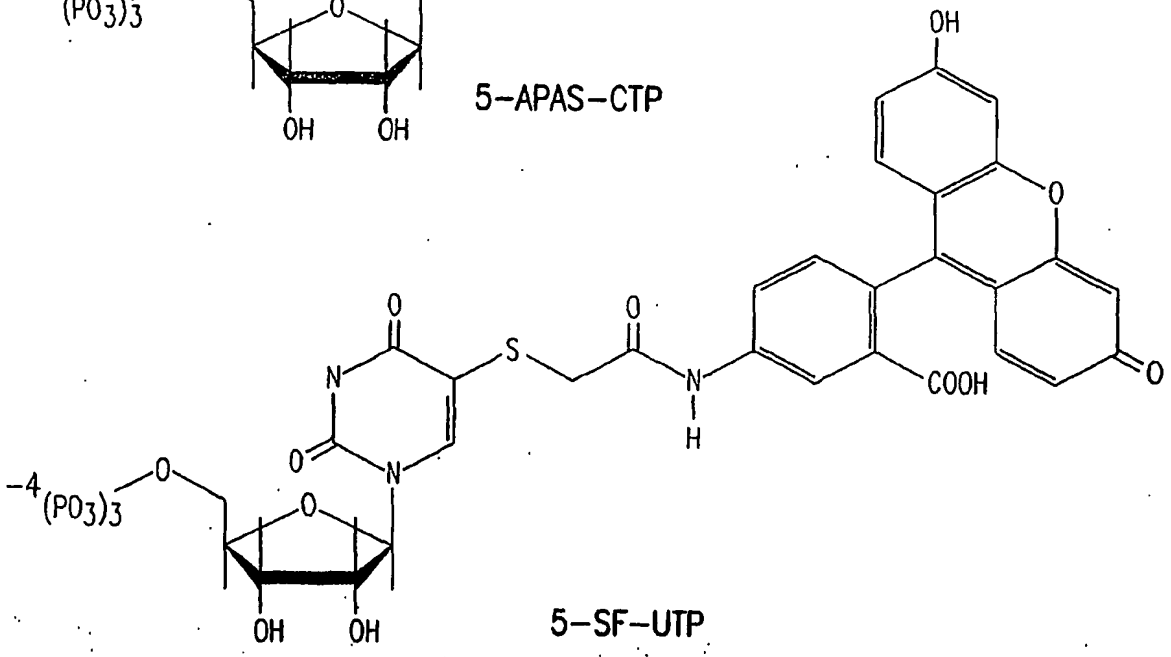
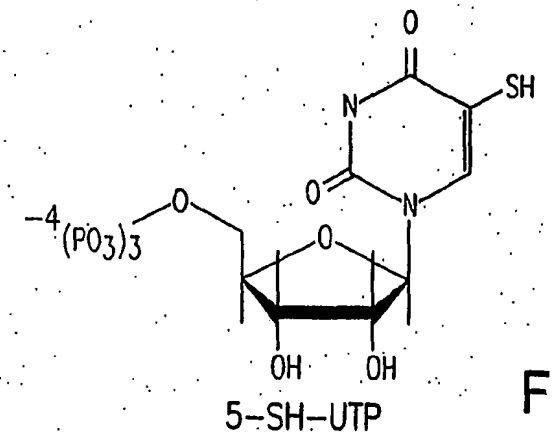

DOUBLE STRANDED OR SINGLE STRANDED DNA OR RNA
OR
n R1-(NI)x-OH
INITIATOR
+
n Y ppp(NE)
ELONGATOR
+
n pppNT-R2
TERMINATOR
n R1-(NI)zpNT-R2
OLIGONUCLEOTIDE PRODUCT
MULTIPLE SIGNALS

FIG.2









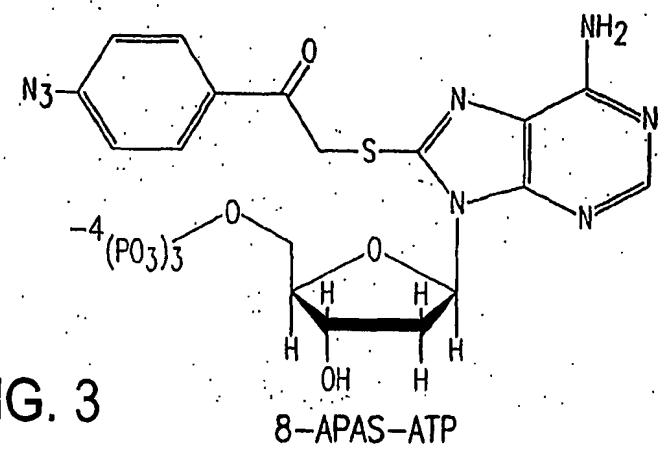


FIG. 3

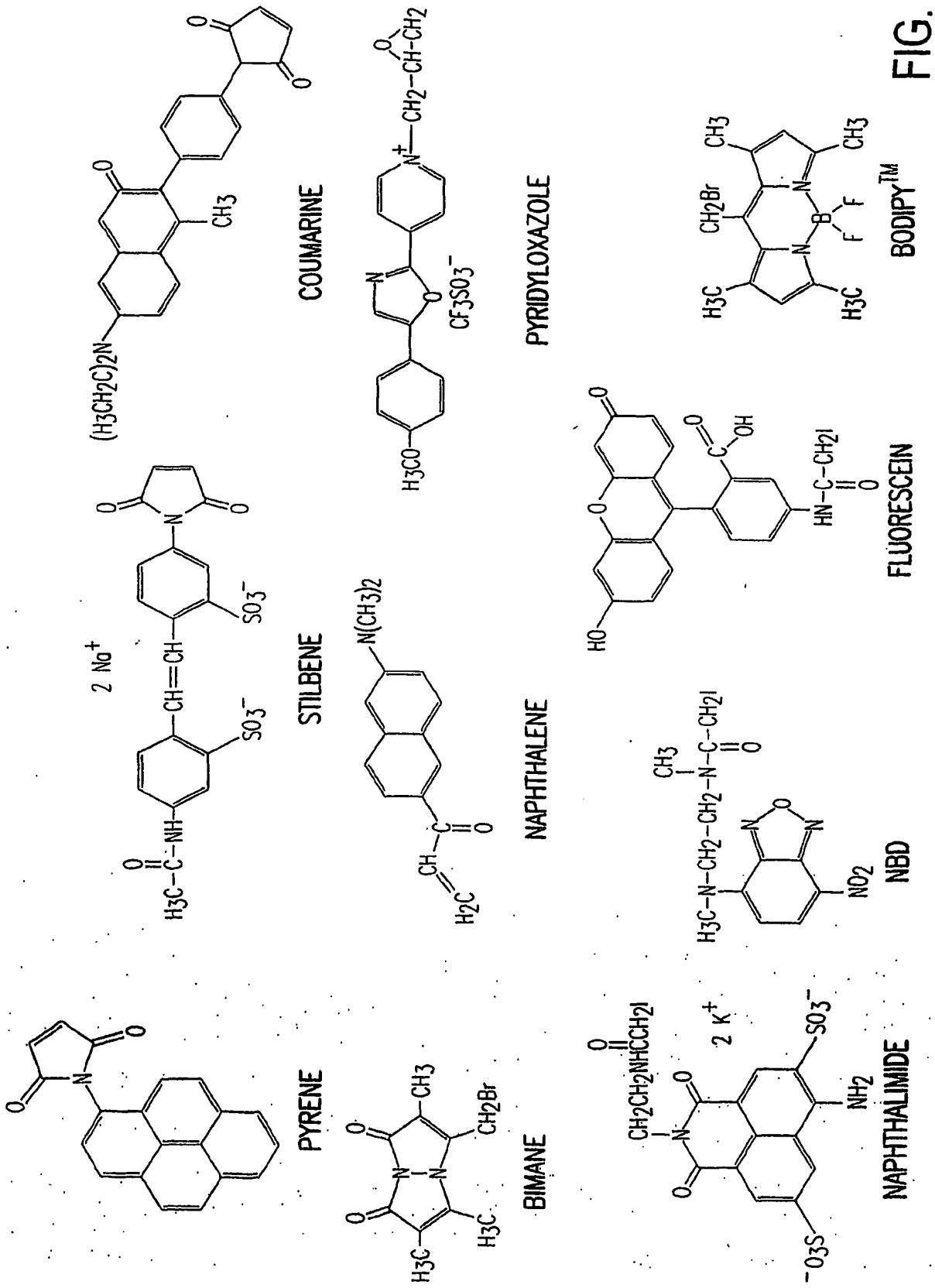

PYRENE
COUMARINE
STILBENE
PYRIDYLOXAZOLE
NAPHTHALENE
FLUORESCEIN
BIMANE
NBD
BODIPY™
NAPHTHALIMIDE

FIG. 4

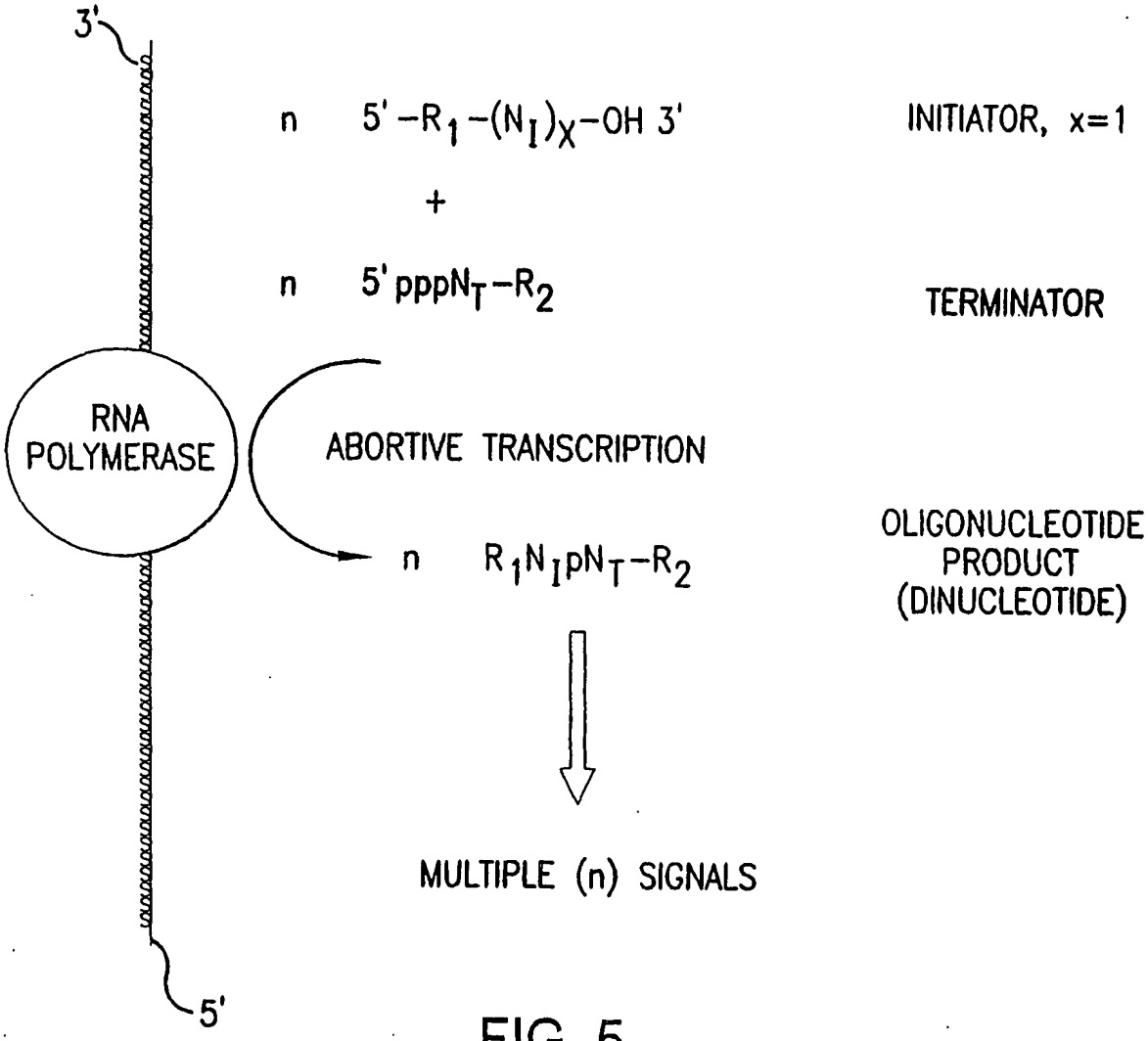

3'
n 5'-R1-(NI)X-OH 3'
INITIATOR, x=1
+
n 5'pppNT-R2
TERMINATOR
RNA POLYMERASE
ABORTIVE TRANSCRIPTION
n R1NIpNT-R2
OLIGONUCLEOTIDE PRODUCT (DINUCLEOTIDE)
MULTIPLE (n) SIGNALS
5'

FIG. 5

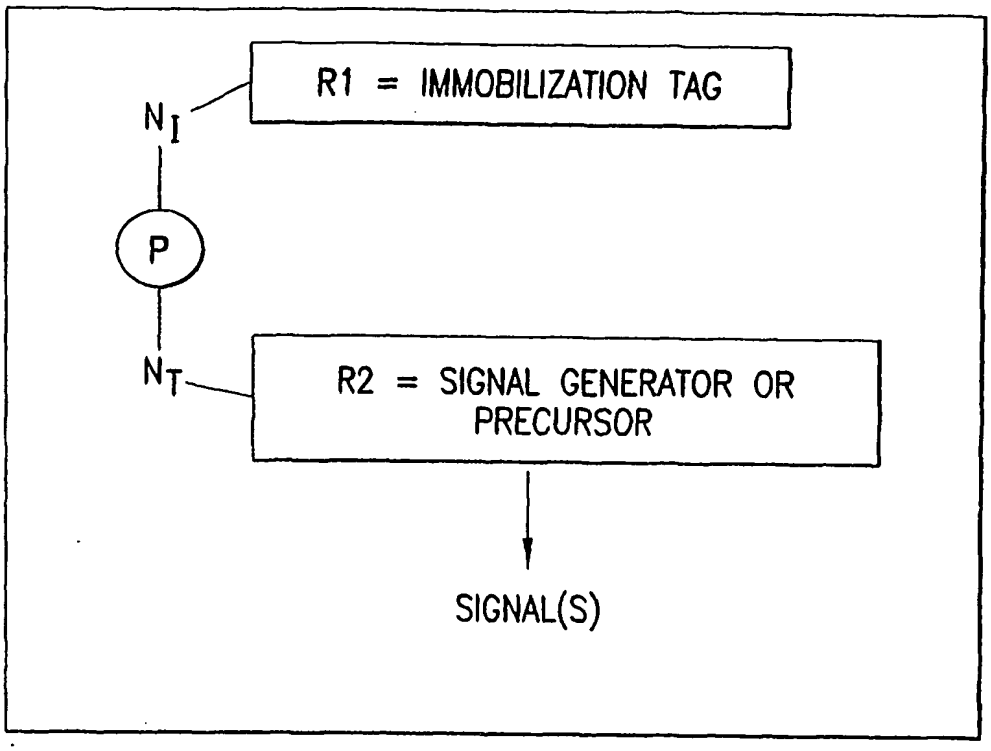

R1 = IMMOBILIZATION TAG
N_I
P
N_T
R2 = SIGNAL GENERATOR OR PRECURSOR
SIGNAL(S)

FIG. 6

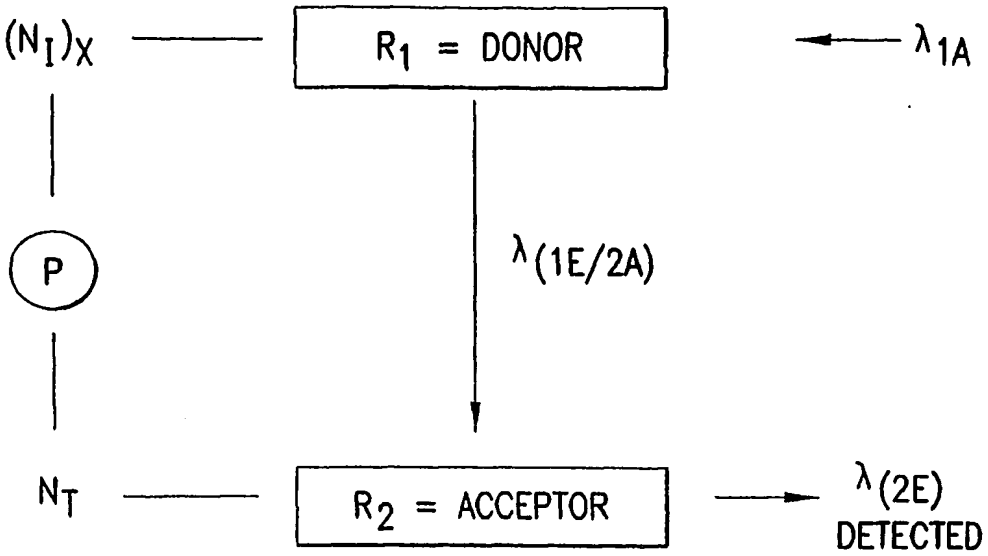

$(N_I)_X$
R_1 = DONOR
λ_{1A}
P
λ(1E/2A)
N_T
R_2 = ACCEPTOR
λ(2E)
DETECTED

FIG. 7

n $R_1N_1pN_2R_2$–OH

+

n $pppN_3R_3$

↓

n $R_1N_1pN_2R_2pN_3R_3$

WHERE N_3 IS A TERMINATOR

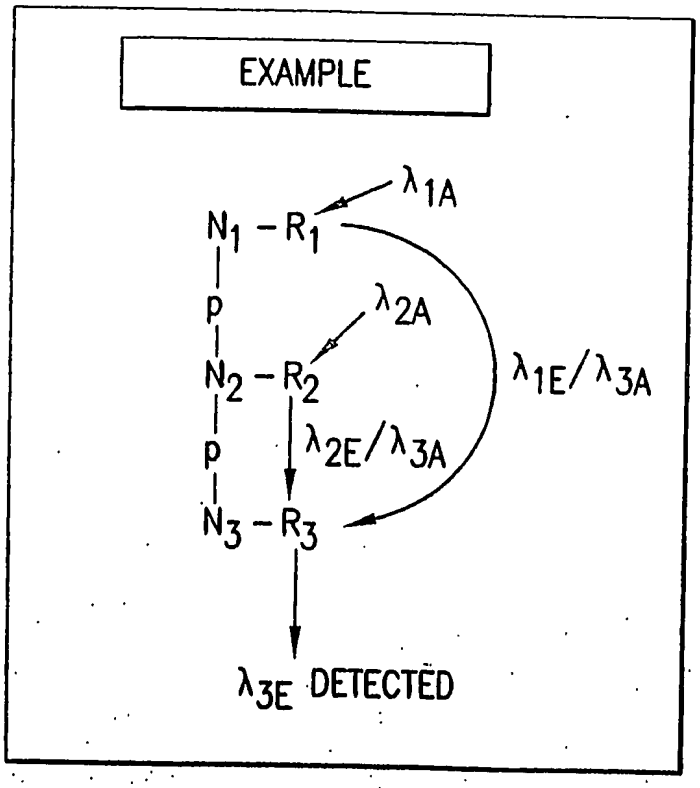


FIG. 8

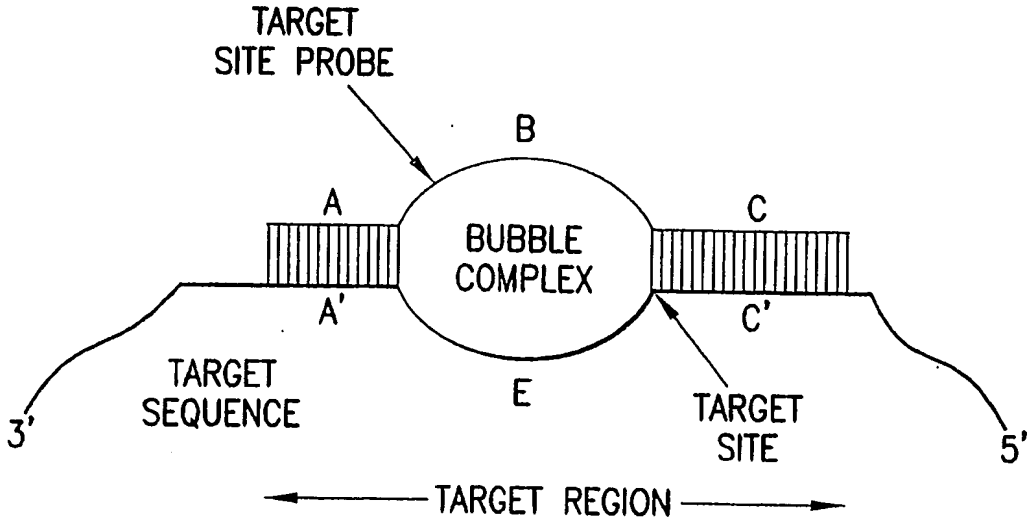

TARGET
SITE PROBE
B
A
C
BUBBLE
COMPLEX
A'
C'
TARGET
SEQUENCE
E
TARGET
SITE
3'
5'
TARGET REGION

FIG. 9

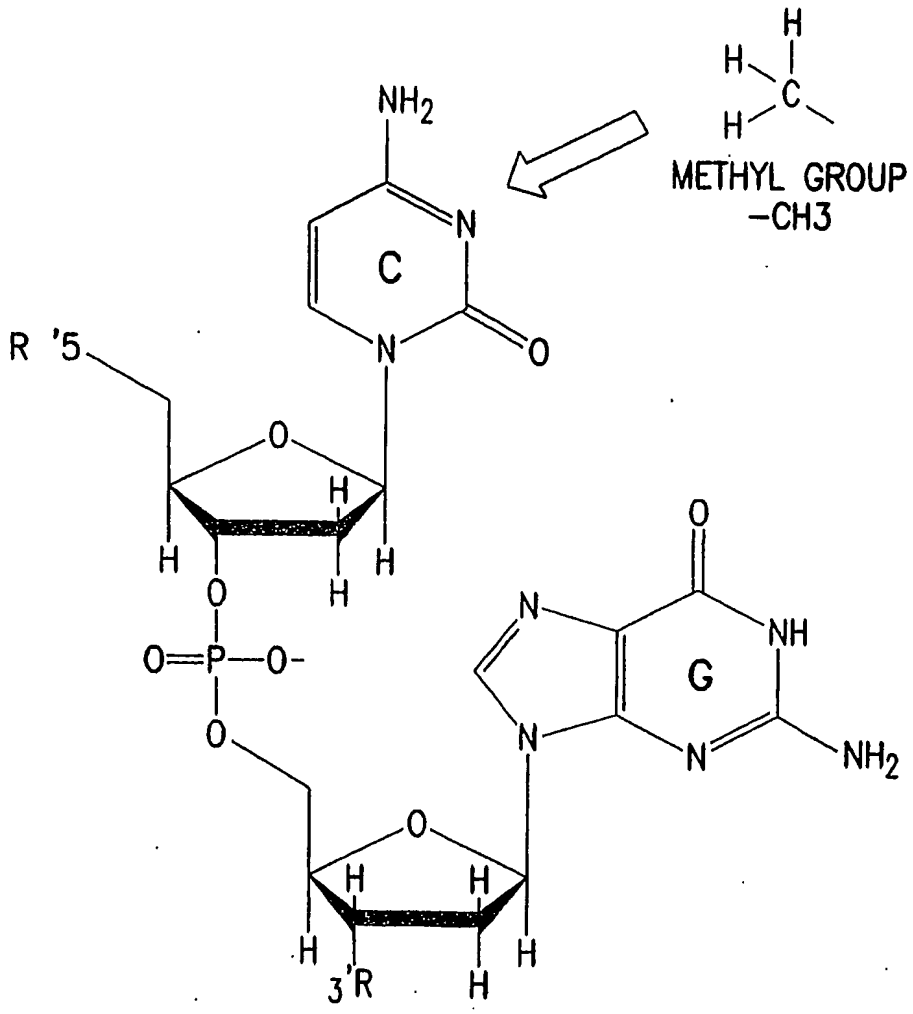


FIG. 10

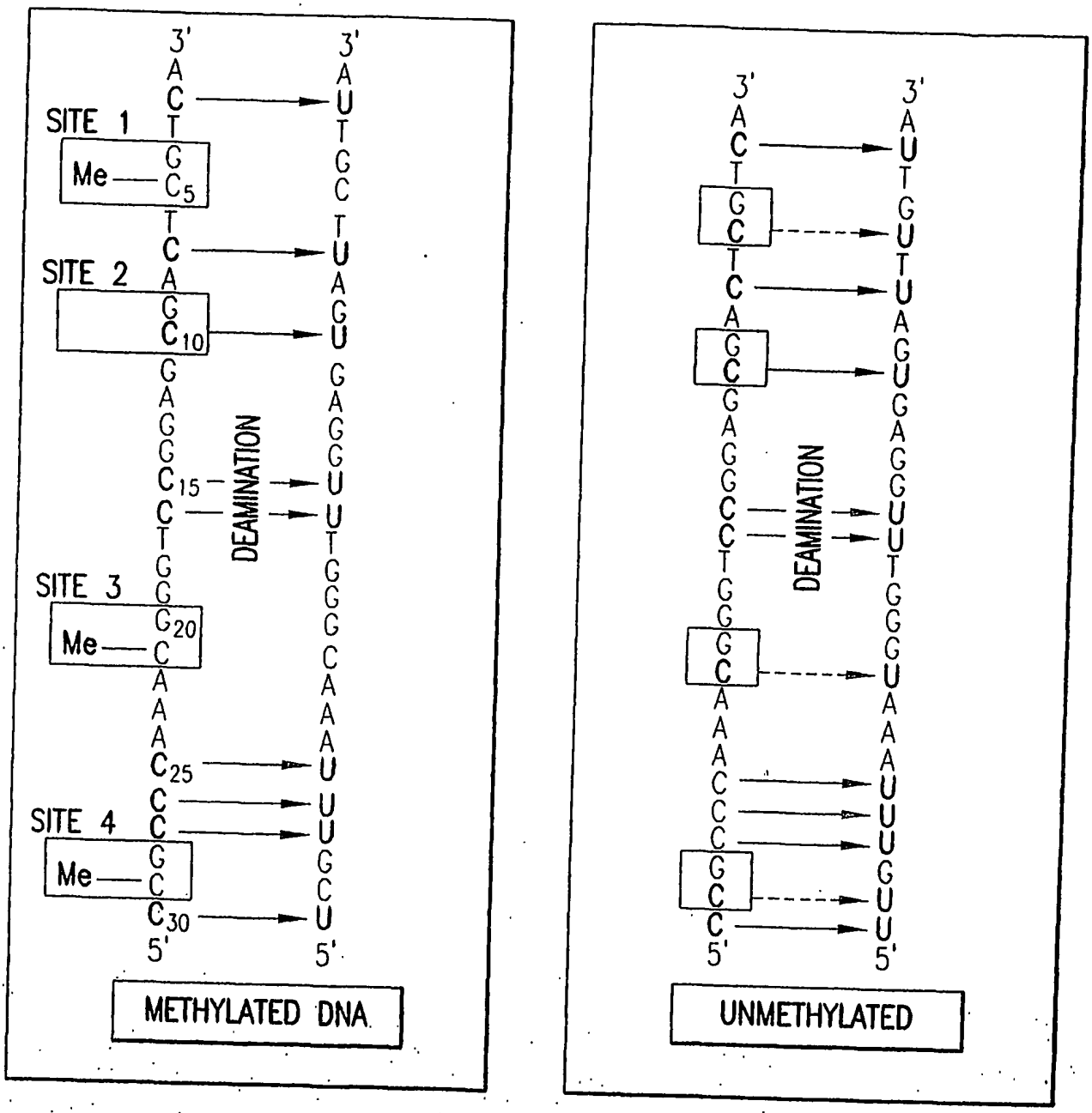

SITE 1
SITE 2
SITE 3
SITE 4
Me
DEAMINATION
METHYLATED DNA
UNMETHYLATED

FIG. 11

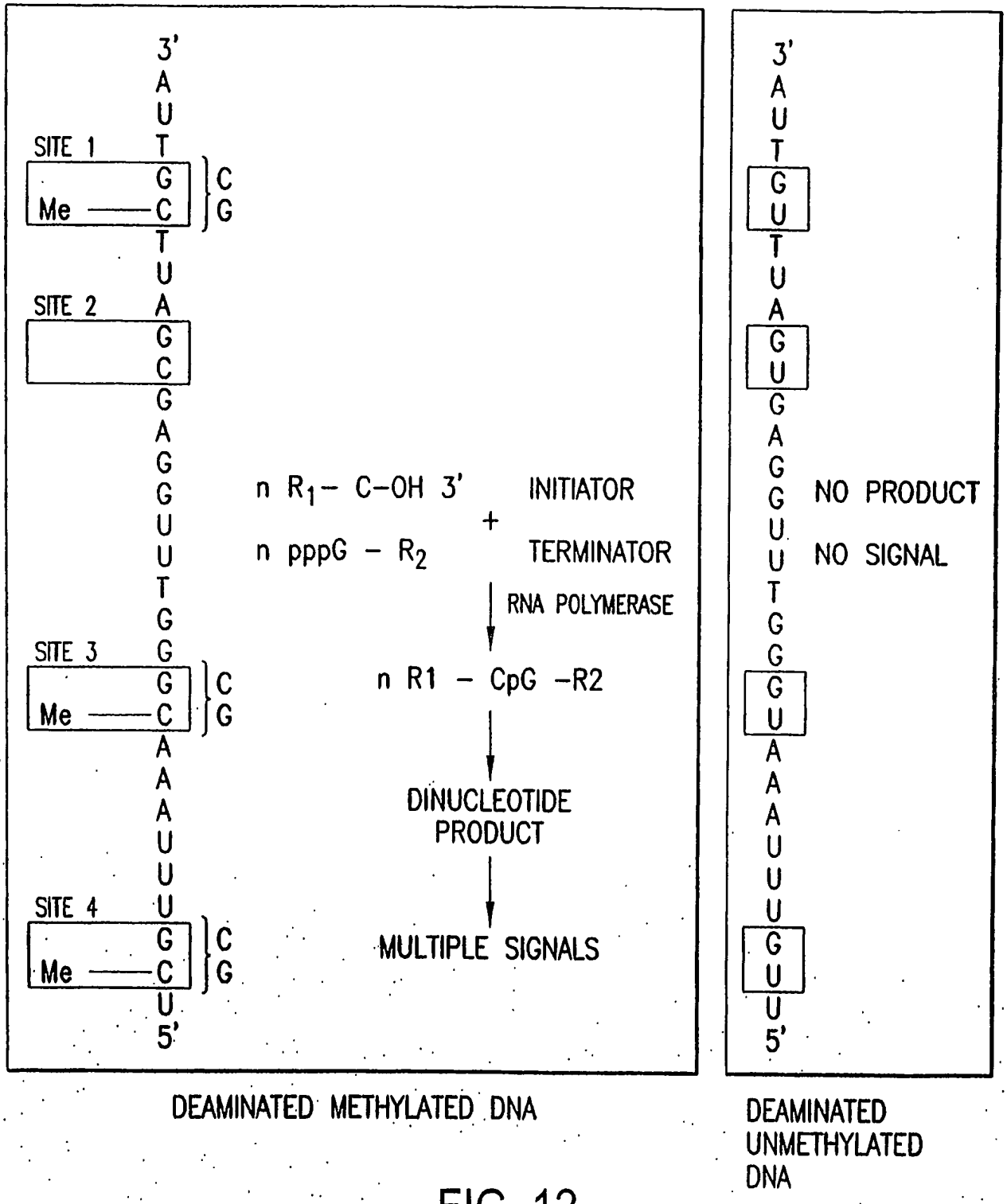

3'
A
U
T
SITE 1
G
Me
C
C
G
T
U
A
SITE 2
G
C
G
A
G
G
U
U
T
G
G
SITE 3
G
Me
C
C
G
A
A
A
U
U
U
SITE 4
G
Me
C
C
G
U
5'
n R1 – C–OH 3'
INITIATOR
+
n pppG – R2
TERMINATOR
RNA POLYMERASE
n R1 – CpG –R2
DINUCLEOTIDE PRODUCT
MULTIPLE SIGNALS
DEAMINATED METHYLATED DNA
3'
A
U
T
G
U
T
U
A
G
U
G
A
G
G
U
U
T
G
G
G
U
A
A
A
U
U
U
G
U
U
5'
NO PRODUCT
NO SIGNAL
DEAMINATED UNMETHYLATED DNA

FIG. 12

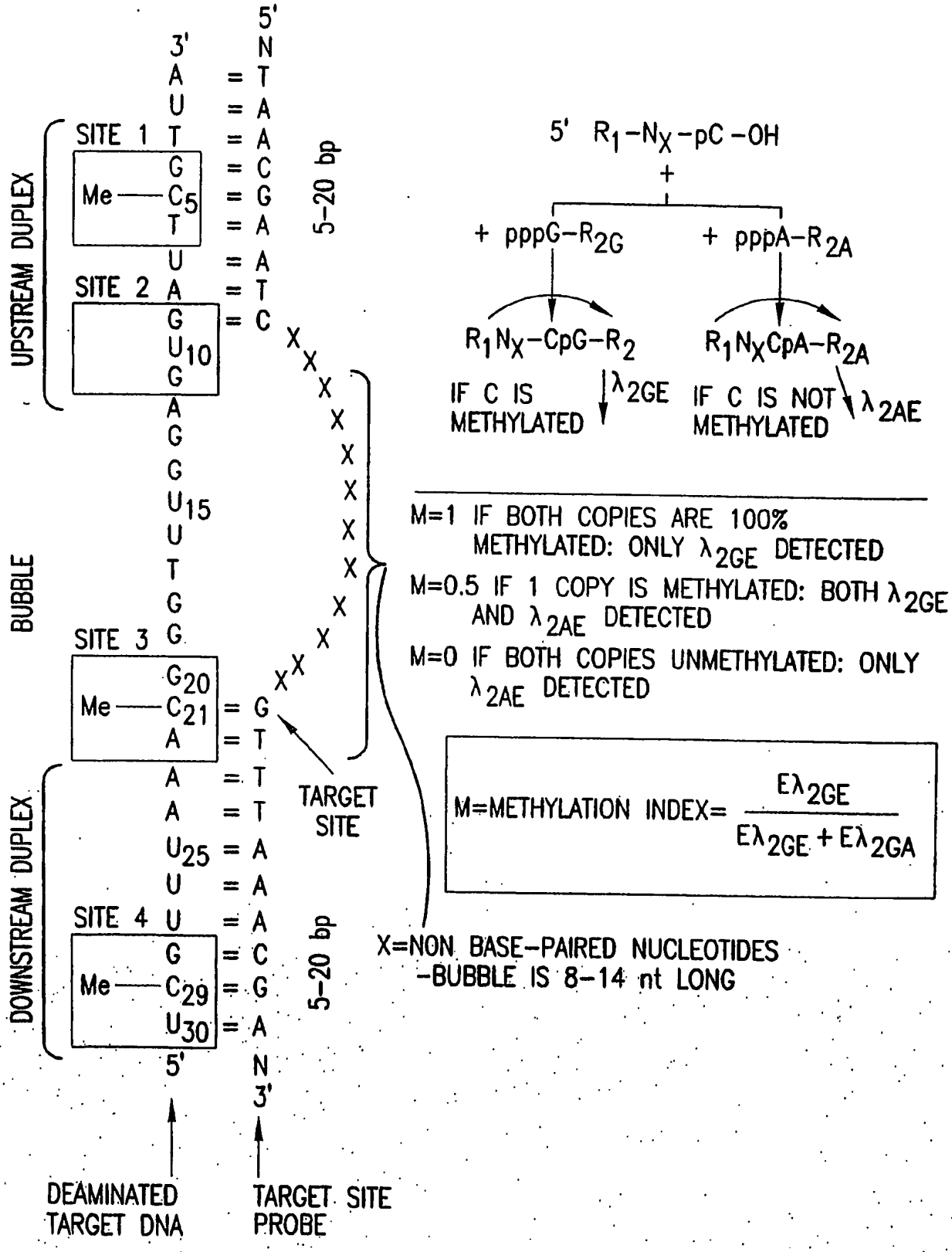

5'
3'
SITE 1
SITE 2
SITE 3
SITE 4
Me
UPSTREAM DUPLEX
BUBBLE
DOWNSTREAM DUPLEX
5–20 bp
5–20 bp
TARGET SITE
DEAMINATED TARGET DNA
TARGET SITE PROBE
5' R1–NX–pC–OH
+ pppG–R2G
+ pppA–R2A
R1NX–CpG–R2
R1NXCpA–R2A
IF C IS METHYLATED
IF C IS NOT METHYLATED
λ2GE
λ2AE
M=1 IF BOTH COPIES ARE 100% METHYLATED: ONLY λ2GE DETECTED
M=0.5 IF 1 COPY IS METHYLATED: BOTH λ2GE AND λ2AE DETECTED
M=0 IF BOTH COPIES UNMETHYLATED: ONLY λ2AE DETECTED
M=METHYLATION INDEX= Eλ2GE / Eλ2GE + Eλ2GA
X=NON BASE-PAIRED NUCLEOTIDES -BUBBLE IS 8-14 nt LONG

FIG. 13

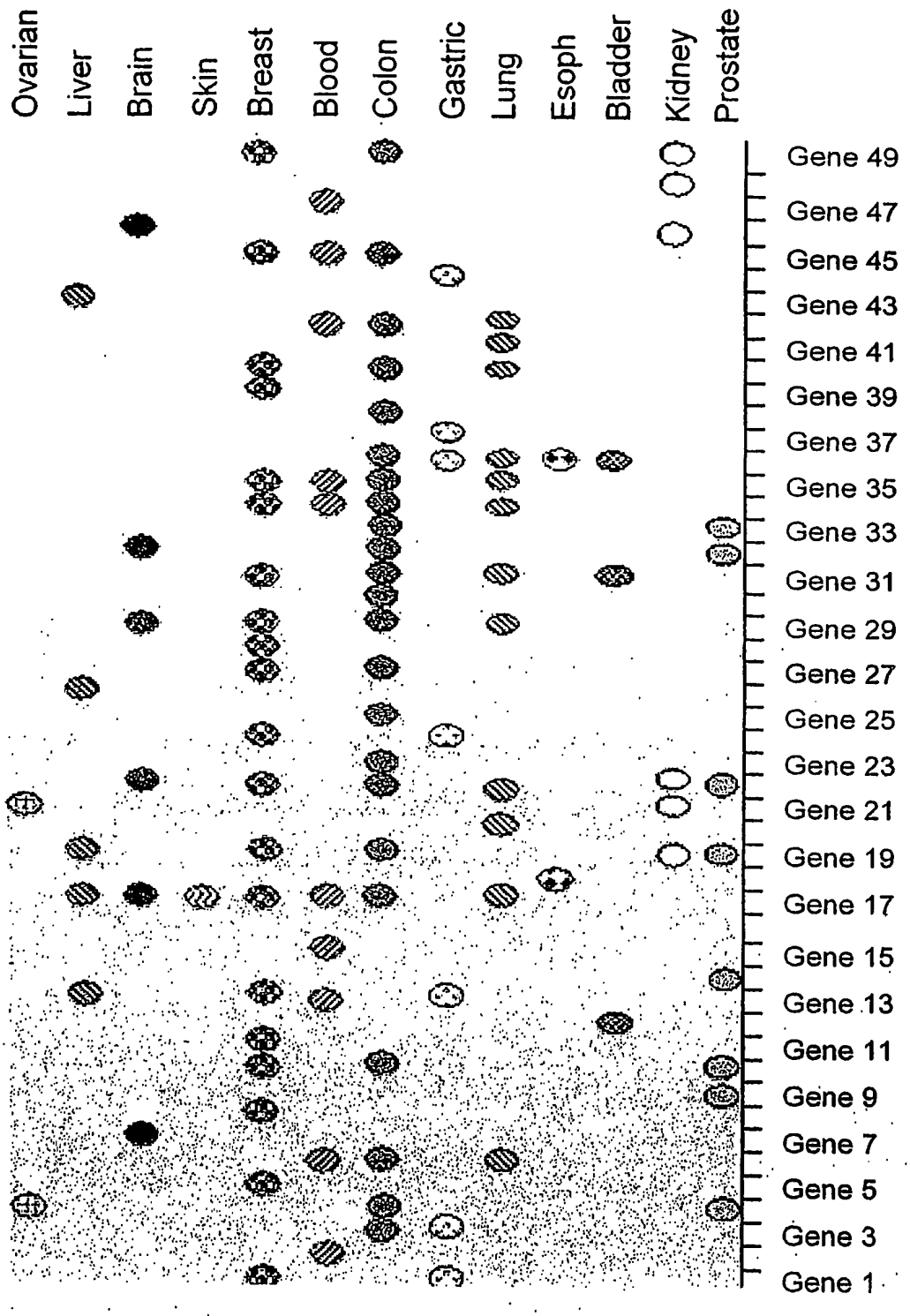

Ovarian
Liver
Brain
Skin
Breast
Blood
Colon
Gastric
Lung
Esoph
Bladder
Kidney
Prostate
Gene 49
Gene 47
Gene 45
Gene 43
Gene 41
Gene 39
Gene 37
Gene 35
Gene 33
Gene 31
Gene 29
Gene 27
Gene 25
Gene 23
Gene 21
Gene 19
Gene 17
Gene 15
Gene 13
Gene 11
Gene 9
Gene 7
Gene 5
Gene 3
Gene 1

FIG. 14

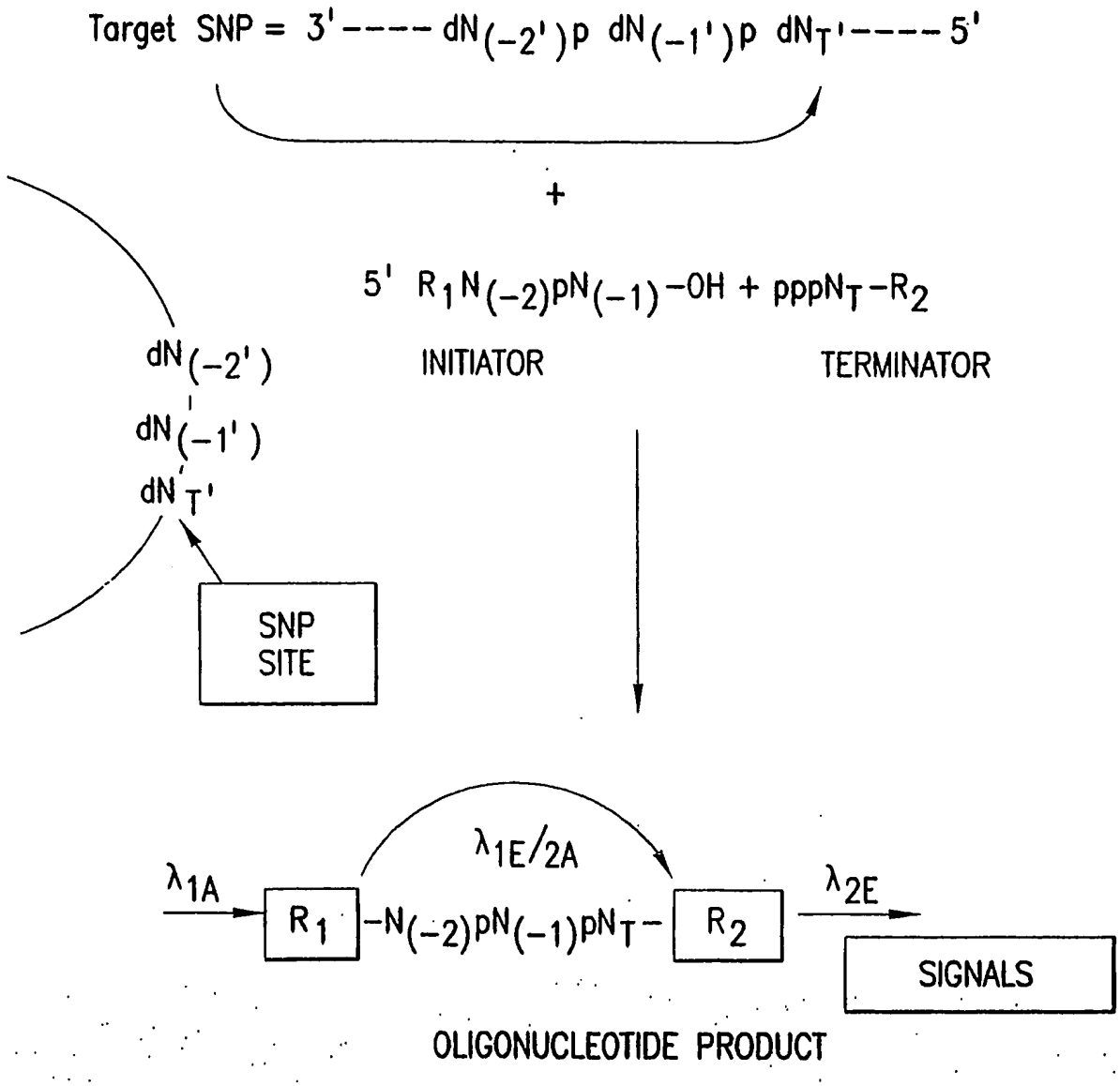

Target SNP = 3'---- dN(-2')p dN(-1')p dNT'---- 5'
+
5' R1N(-2)pN(-1)-OH + pppNT-R2
INITIATOR
TERMINATOR
dN(-2')
dN(-1')
dN'T'
SNP SITE
λ1E/2A
λ1A
R1
-N(-2)pN(-1)pNT-
R2
λ2E
SIGNALS
OLIGONUCLEOTIDE PRODUCT

FIG. 15

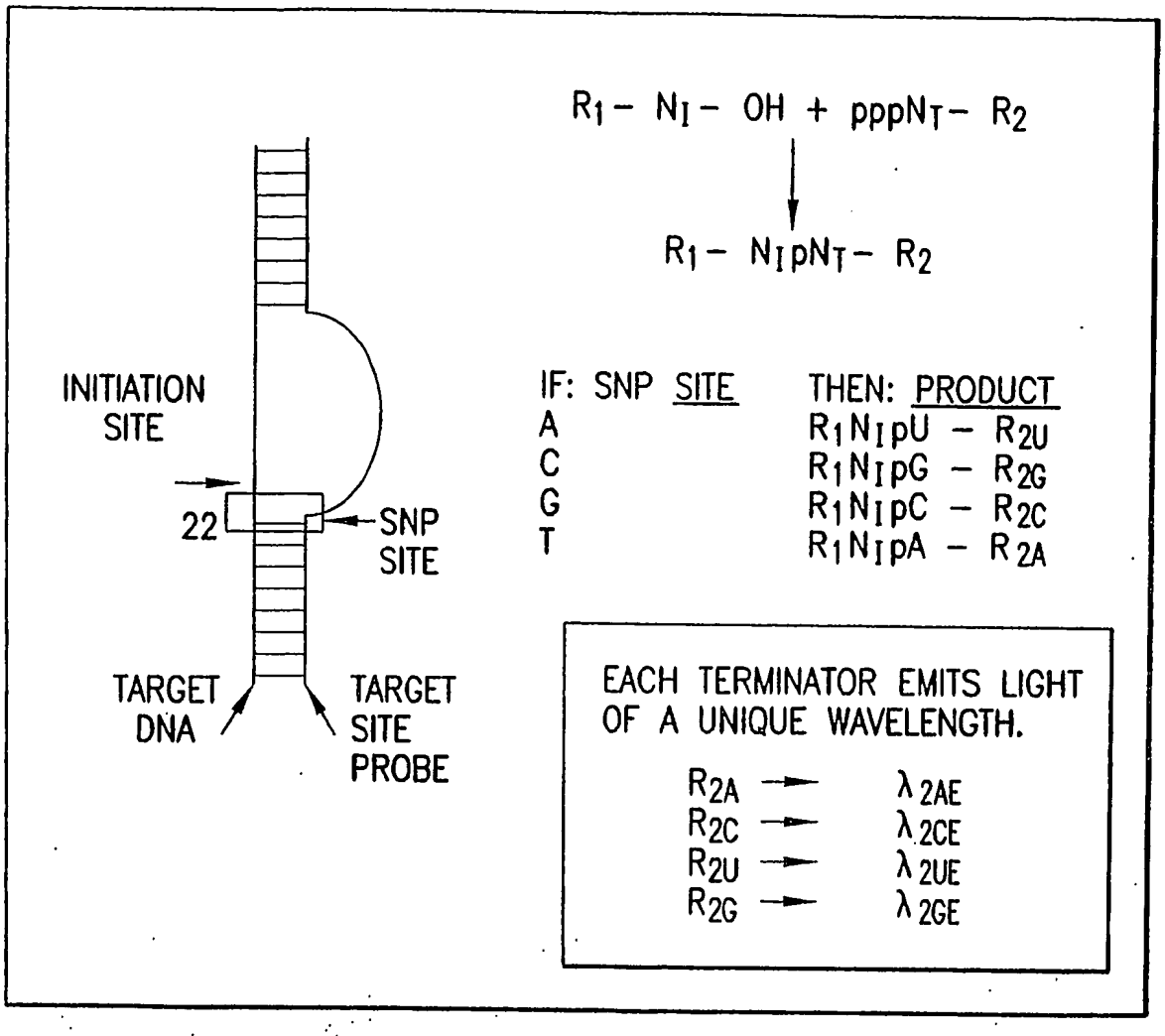
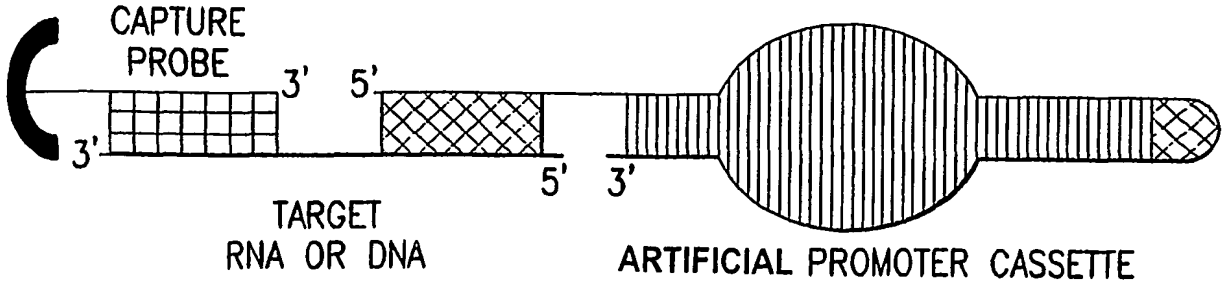

$R_1 - N_I - OH + pppN_T - R_2$
$R_1 - N_I pN_T - R_2$
INITIATION SITE
22
SNP SITE
TARGET DNA
TARGET SITE PROBE
IF: SNP SITE
A
C
G
T
THEN: PRODUCT
$R_1N_IpU - R_{2U}$
$R_1N_IpG - R_{2G}$
$R_1N_IpC - R_{2C}$
$R_1N_IpA - R_{2A}$
EACH TERMINATOR EMITS LIGHT OF A UNIQUE WAVELENGTH.
$R_{2A} \rightarrow \lambda_{2AE}$
$R_{2C} \rightarrow \lambda_{2CE}$
$R_{2U} \rightarrow \lambda_{2UE}$
$R_{2G} \rightarrow \lambda_{2GE}$

FIG. 16


CAPTURE PROBE
3'
5'
3'
5'
3'
TARGET RNA OR DNA
ARTIFICIAL PROMOTER CASSETTE

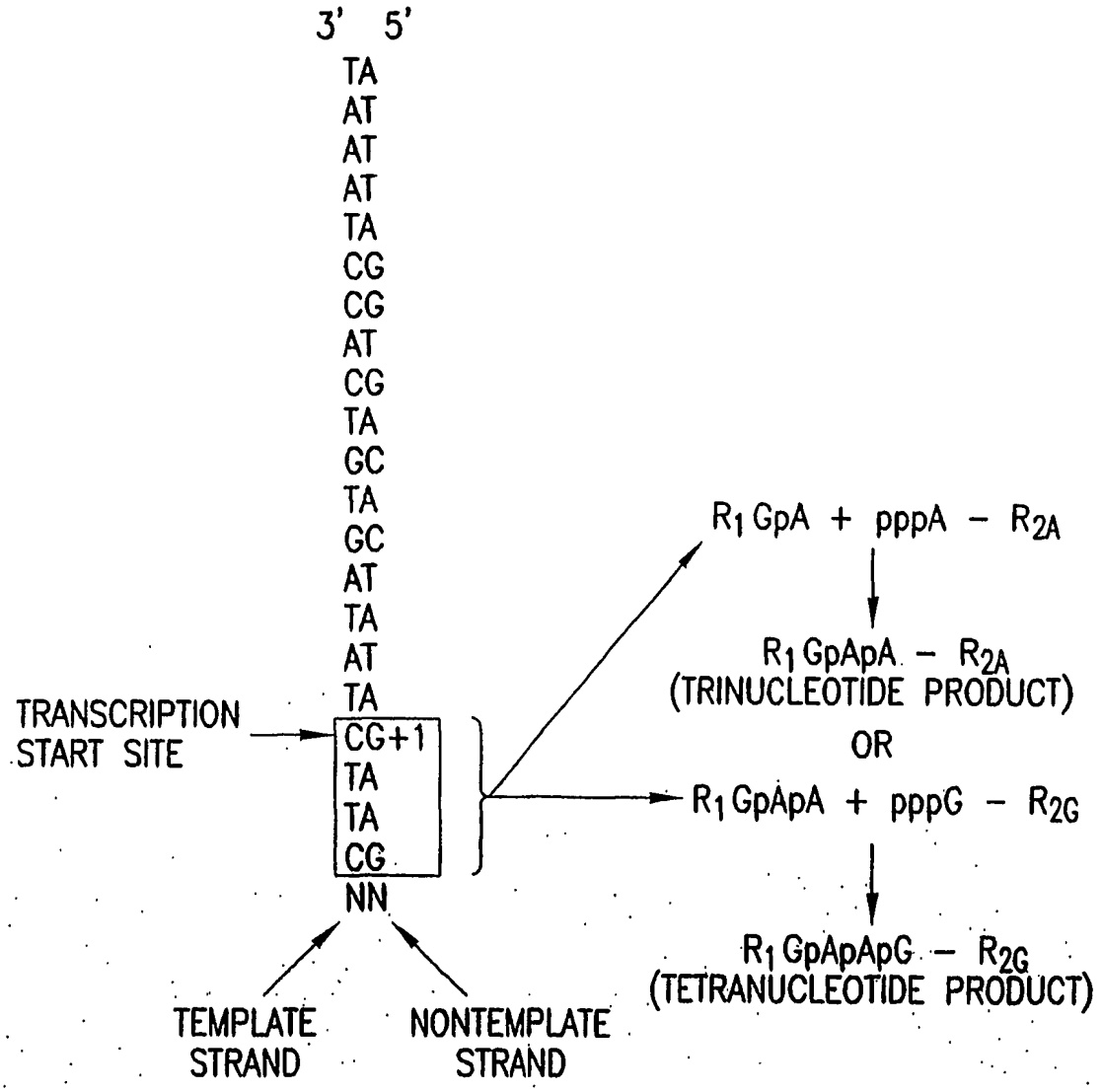

3' 5'
TA
AT
AT
AT
TA
CG
CG
AT
CG
TA
GC
TA
GC
AT
TA
AT
TA
TRANSCRIPTION START SITE
CG+1
TA
TA
CG
NN
TEMPLATE STRAND
NONTEMPLATE STRAND
R1 GpA + pppA – R2A
R1 GpApA – R2A
(TRINUCLEOTIDE PRODUCT)
OR
R1 GpApA + pppG – R2G
R1 GpApApG – R2G
(TETRANUCLEOTIDE PRODUCT)

FIG. 17

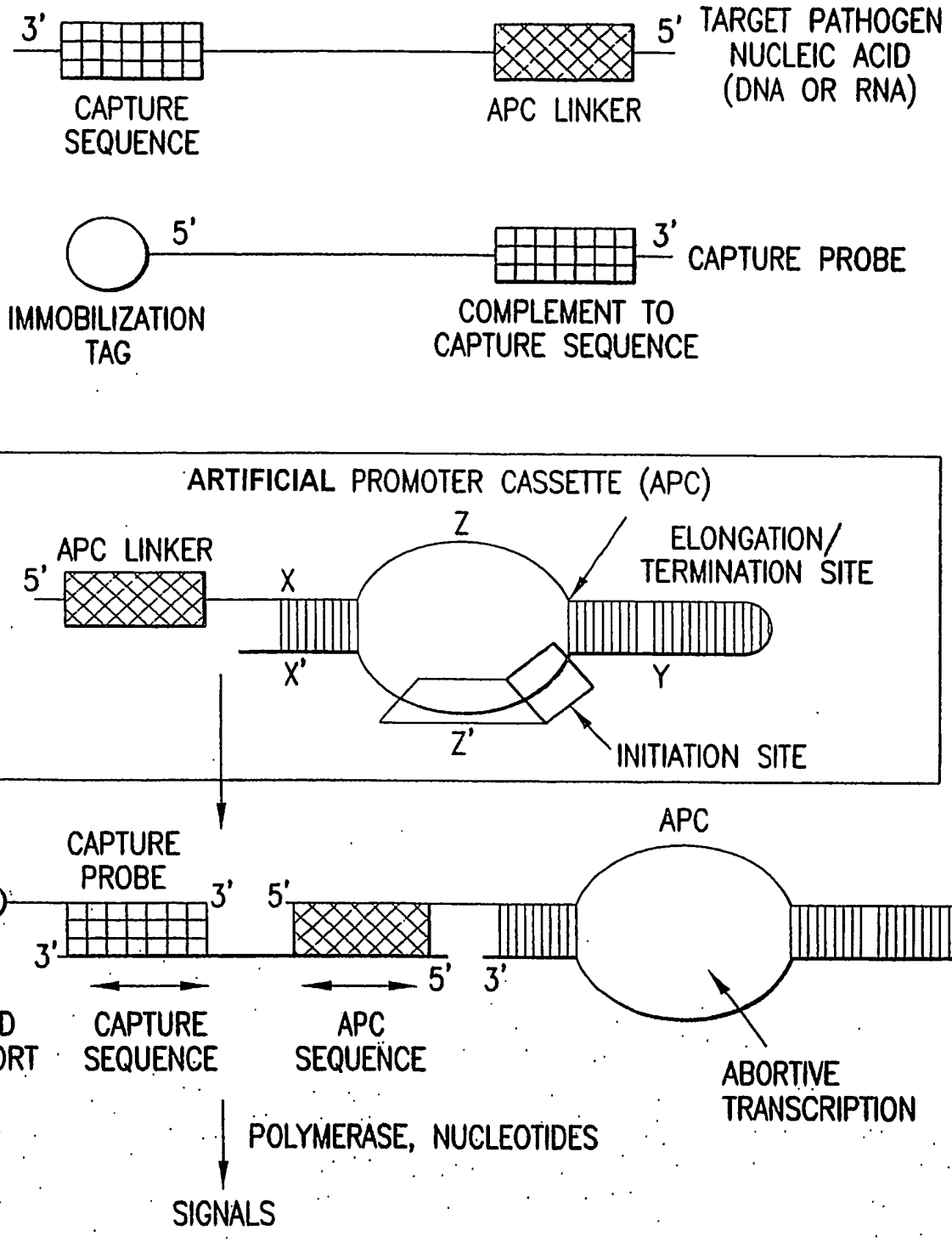

3'
5'
TARGET PATHOGEN NUCLEIC ACID (DNA OR RNA)
CAPTURE SEQUENCE
APC LINKER
5'
3'
CAPTURE PROBE
IMMOBILIZATION TAG
COMPLEMENT TO CAPTURE SEQUENCE
ARTIFICIAL PROMOTER CASSETTE (APC)
APC LINKER
5'
X
Z
ELONGATION/ TERMINATION SITE
X'
Y
Z'
INITIATION SITE
APC
CAPTURE PROBE
3'
5'
3'
5'
3'
SOLID SUPPORT
CAPTURE SEQUENCE
APC SEQUENCE
ABORTIVE TRANSCRIPTION
POLYMERASE, NUCLEOTIDES
SIGNALS

FIG. 18

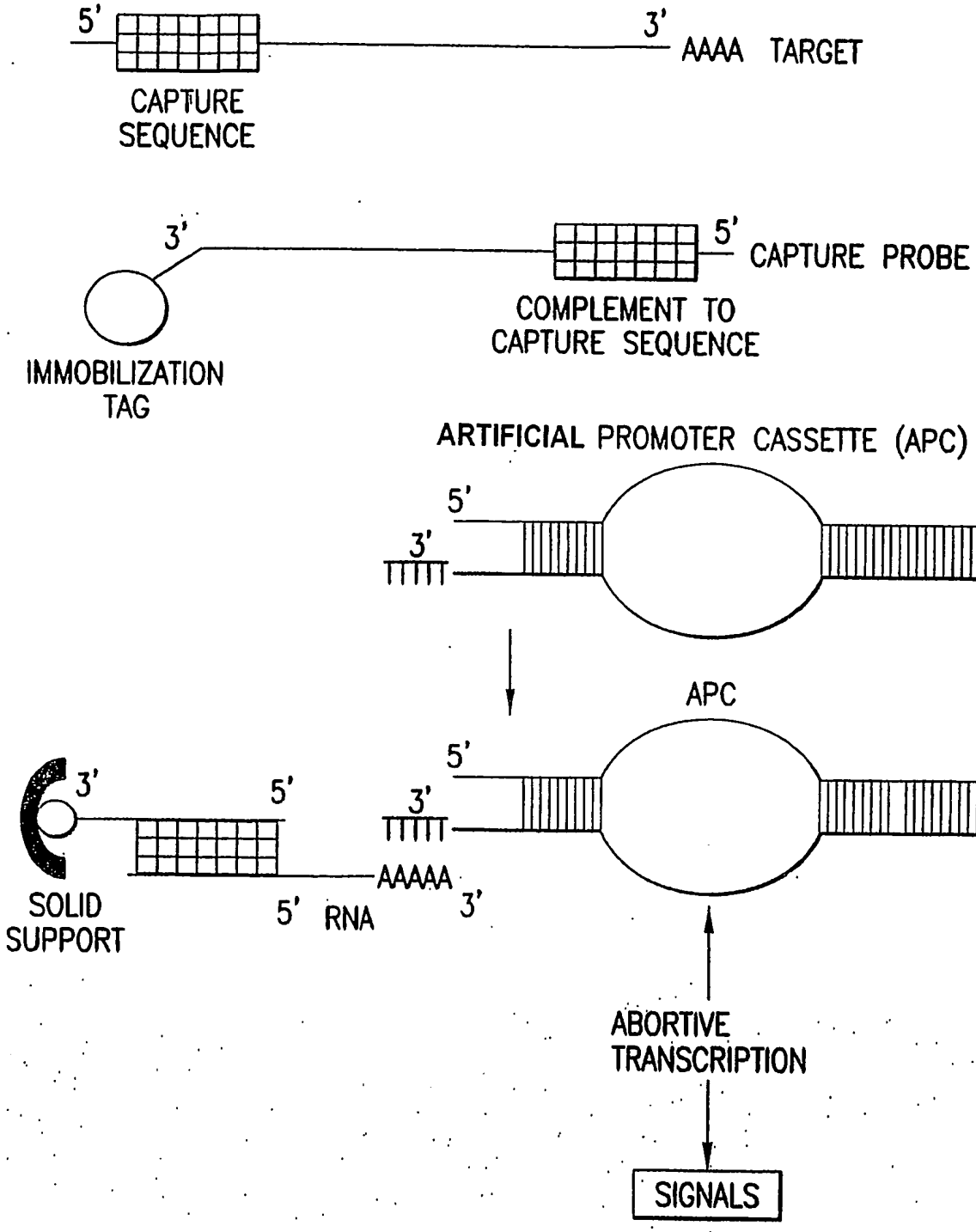

5'
3'
AAAA TARGET
CAPTURE SEQUENCE
3'
5'
CAPTURE PROBE
COMPLEMENT TO CAPTURE SEQUENCE
IMMOBILIZATION TAG
ARTIFICIAL PROMOTER CASSETTE (APC)
5'
3'
APC
5'
3'
3'
5'
AAAAA
SOLID SUPPORT
5' RNA
3'
ABORTIVE TRANSCRIPTION
SIGNALS

FIG. 19

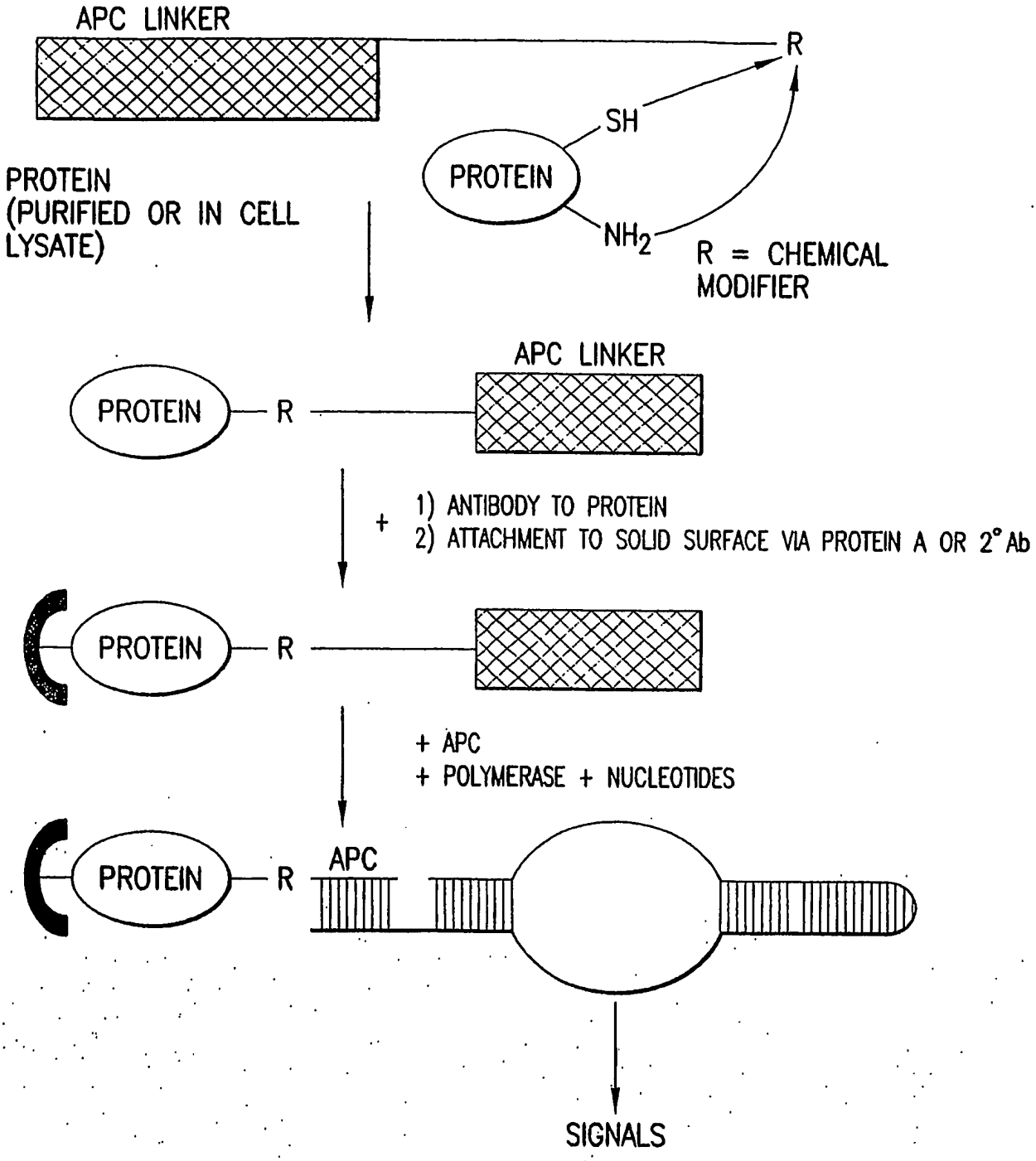

APC LINKER
R
SH
PROTEIN
PROTEIN
(PURIFIED OR IN CELL
LYSATE)
NH2
R = CHEMICAL
MODIFIER
APC LINKER
PROTEIN
R
+
1) ANTIBODY TO PROTEIN
2) ATTACHMENT TO SOLID SURFACE VIA PROTEIN A OR 2° Ab
PROTEIN
R
+ APC
+ POLYMERASE + NUCLEOTIDES
PROTEIN
R
APC
SIGNALS

FIG. 20

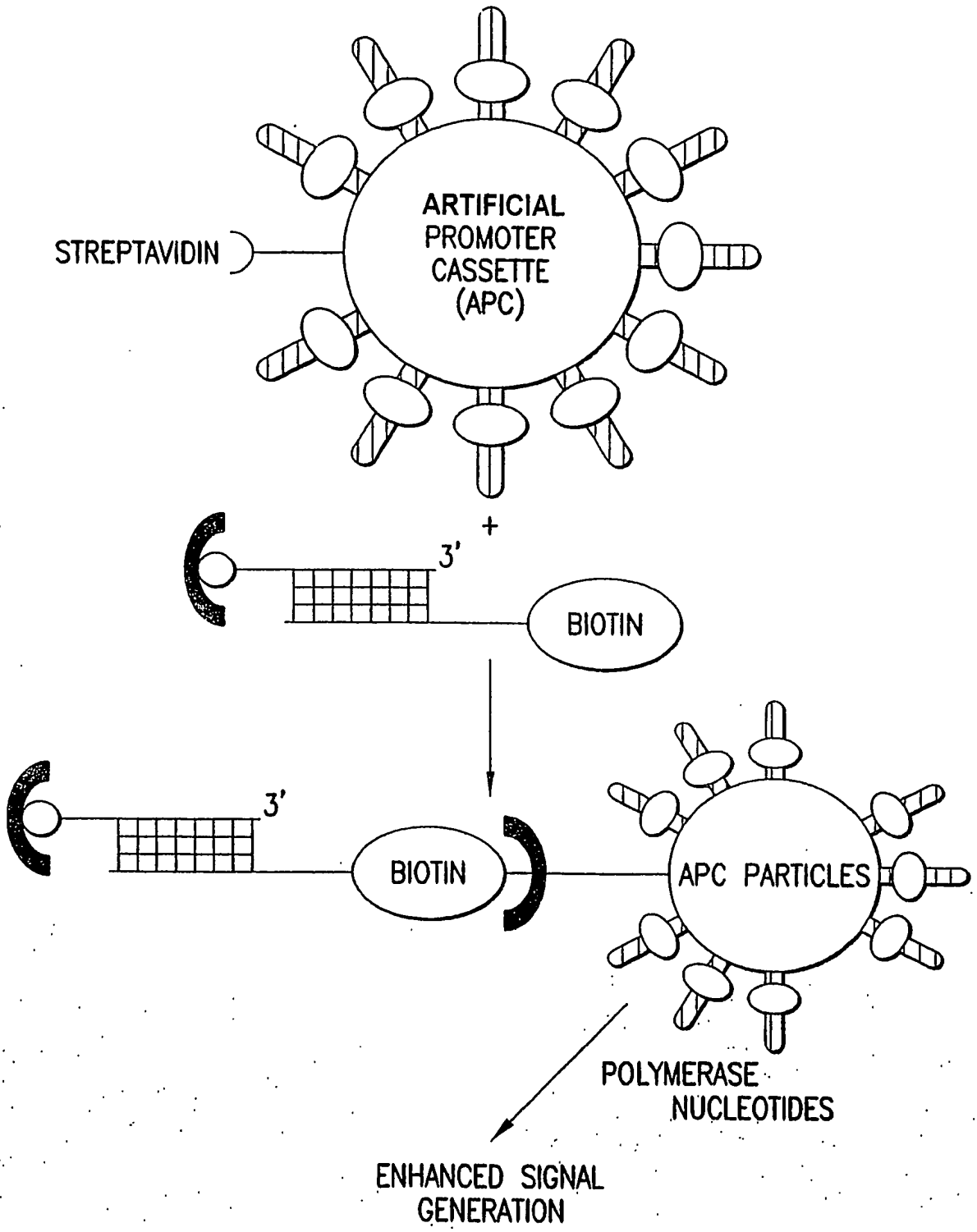

ARTIFICIAL
PROMOTER
CASSETTE
(APC)
STREPTAVIDIN
+
3'
BIOTIN
3'
BIOTIN
APC PARTICLES
POLYMERASE
NUCLEOTIDES
ENHANCED SIGNAL
GENERATION

FIG. 21

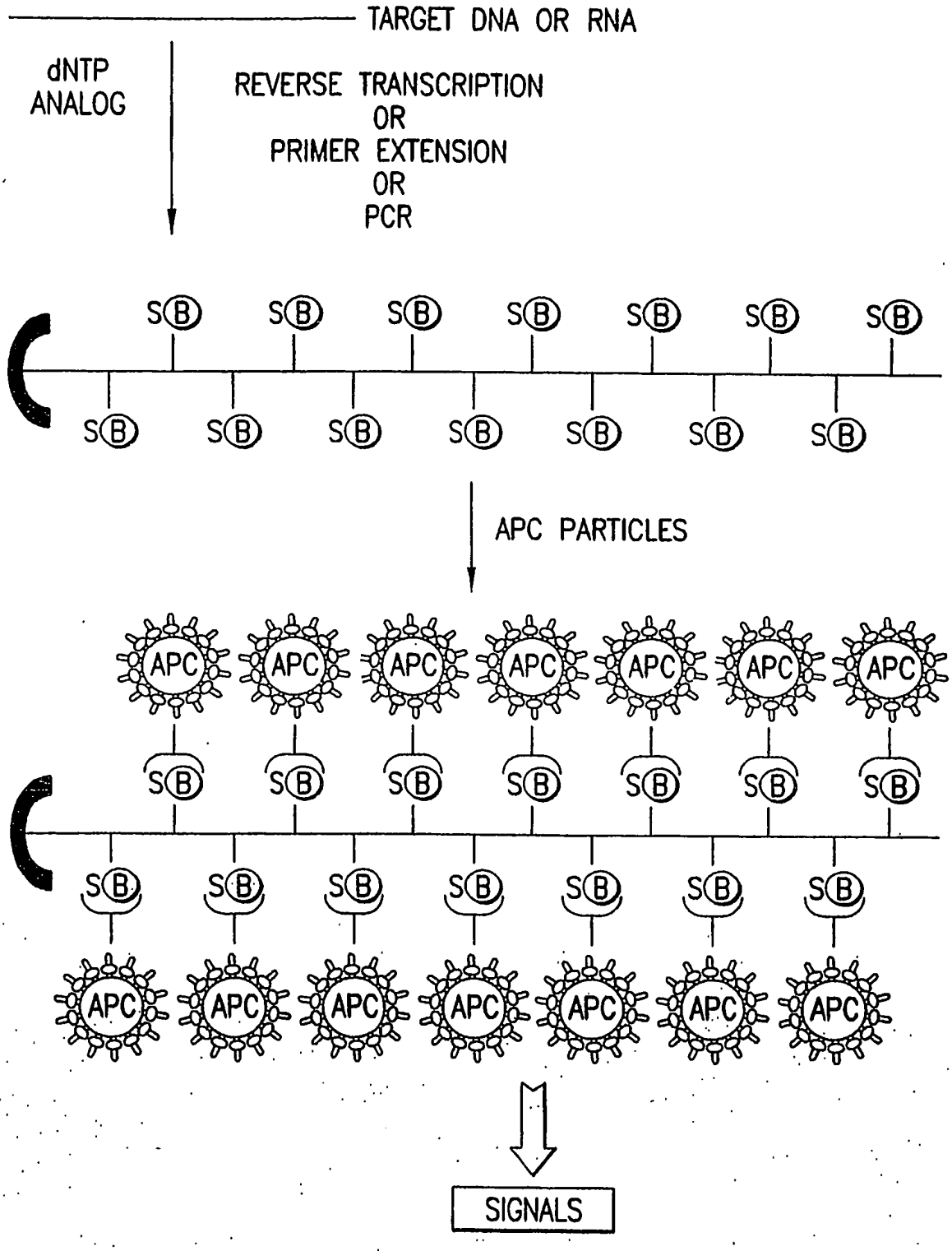

TARGET DNA OR RNA
dNTP ANALOG
REVERSE TRANSCRIPTION OR PRIMER EXTENSION OR PCR
S B
APC PARTICLES
APC
SIGNALS

FIG. 22

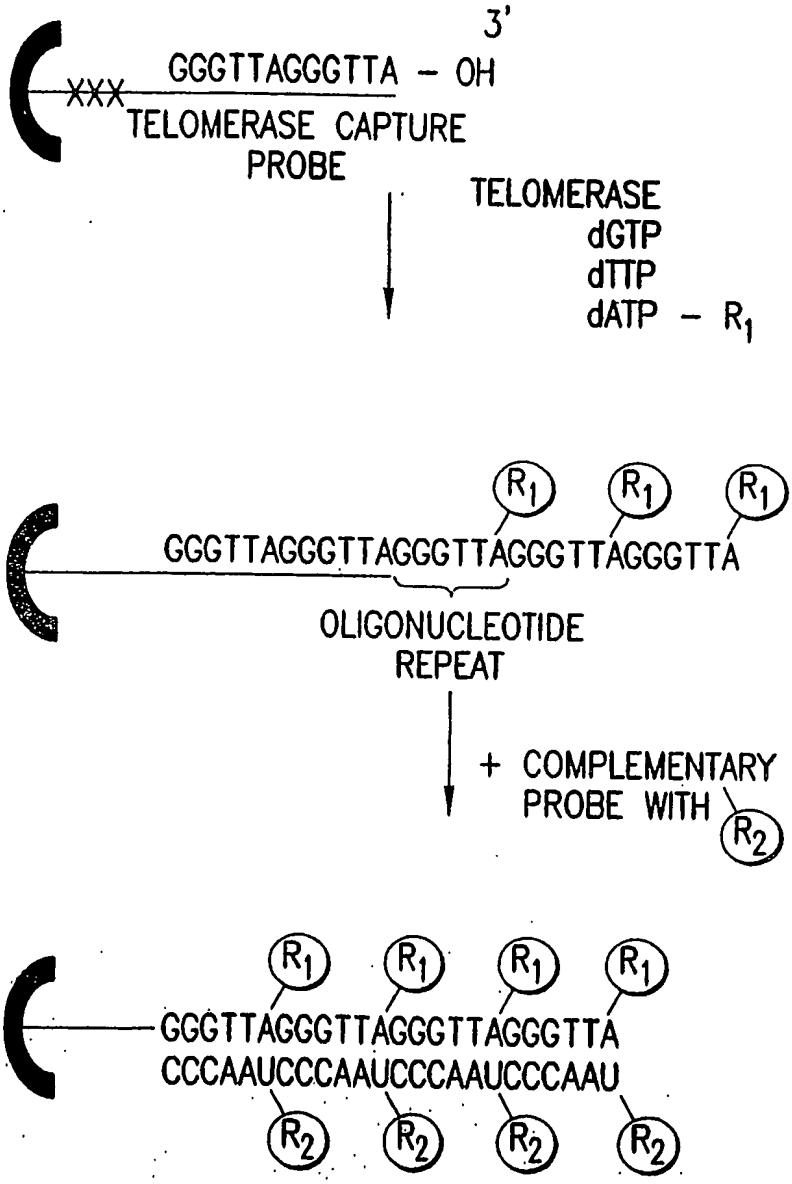
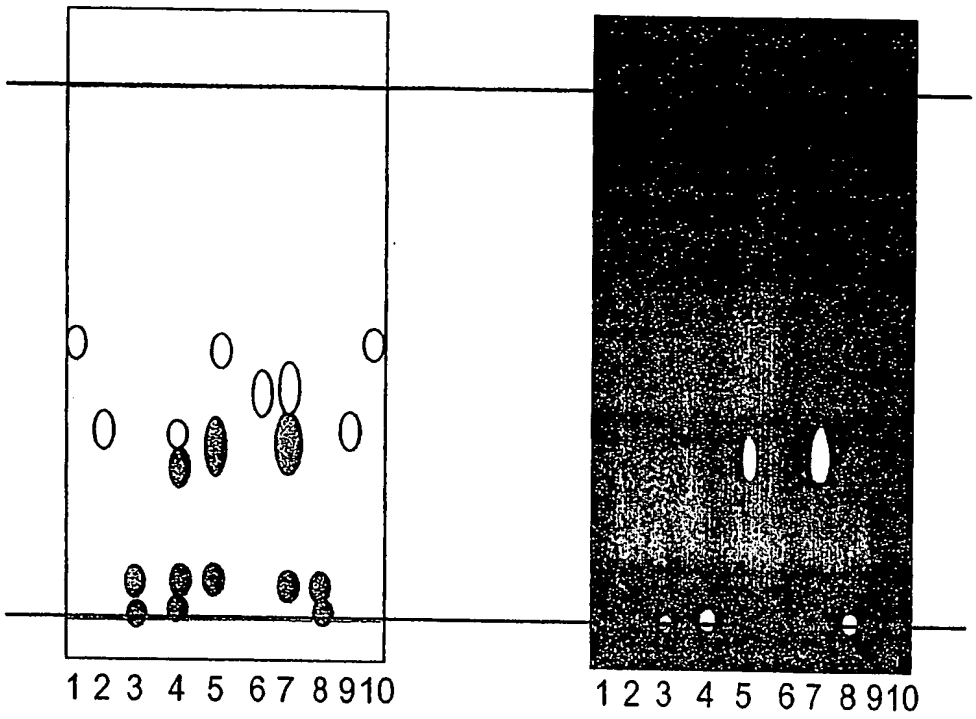

3'
GGGTTAGGGTTA – OH
XXX
TELOMERASE CAPTURE PROBE
TELOMERASE
dGTP
dTTP
dATP – R1
R1 R1 R1
GGGTTAGGGTTAGGGTTAGGGTTAGGGTTA
OLIGONUCLEOTIDE REPEAT
+ COMPLEMENTARY PROBE WITH R2
R1 R1 R1 R1
GGGTTAGGGTTAGGGTTAGGGTTA
CCCAAUCCCAAUCCCAAUCCCAAU
R2 R2 R2 R2

FIG. 23



Lane 1 CMPS
Lane 2 CTPS
Lane 3 IAEDANS
Lane 4 AEDANS-SpppC
Lane 5 AEDANS-S-pC
Lane 6 AMPS
Lane 7 AEDANS-SpA
Lane 8 IAEDANS
Lane 9 CTPS
Lane 10 CMPS

FIG. 24

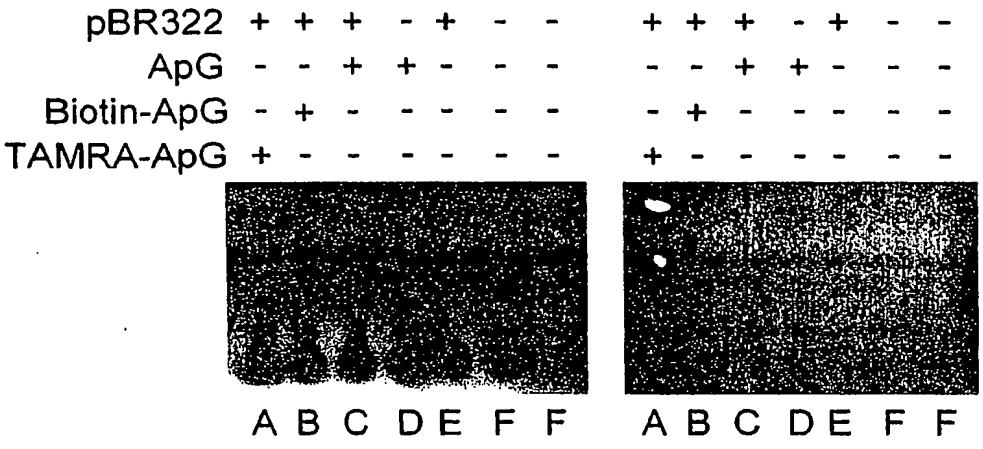


FIG. 25

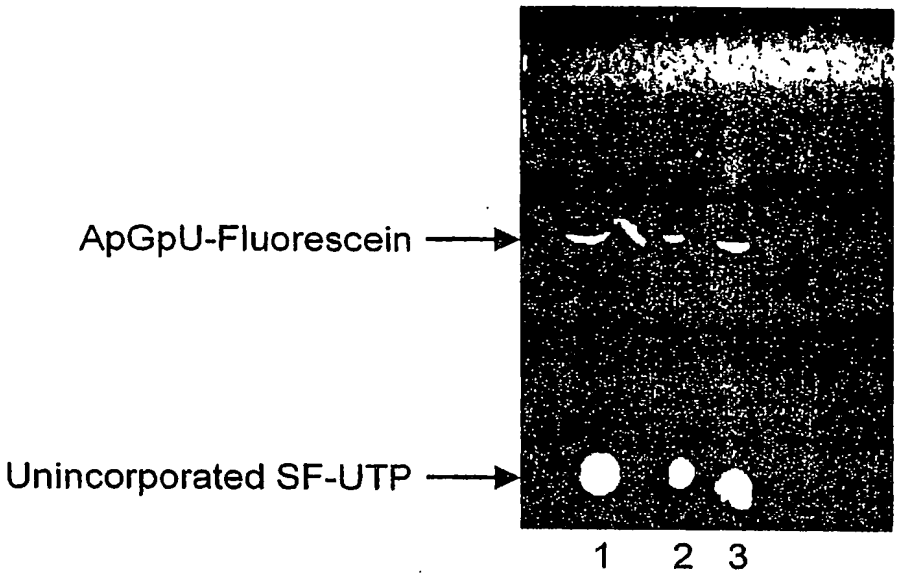


FIG. 26

ATATACTGGGTCTACAAGGTTTAAGTCAACCAGGGATTGAAATATAACTTTTAAACAGAGCTGGATTATCCAGT
AGGCAGATTAAGCATGTGCTTAAGGCATCAGCAAAGTCTGAGCAATCCATTTTTTAAAACGTAGTACATGTTTT
TGATAAGCTTAAAAAGTAGTAGTCACAGGAAAAATTAGAACTTTTACCTCCTTGCGCTTGTTATACTCTTTAGT
GCTGTTTAACTTTTCTTTGTAAGTGAGGGTGGTGGAGGGTGCCCATAATCTTTTCAGGGAGTAAGTTCTTCTT
GGTCTTTCTTTCTTTCTTTCTTTCTTTTTTTCTTGAGACCAAGTTTCGCTCTTGTCTCCCAGGCTGGAGTGCAA
TGGCGCGATCTCGGCTCACTGCAACCTCCGCCTTCTCCTGGGTTCAAGCGATTCTCCTACATCAGCCTCCGA
GTAGCTGGGATTACAGGCATGCGCCACCAAGCCCCGCTAATTTTGTATTTTTTAGTAGAGACAGGGTTTCGC
CATGTTGGTCAGGCTTGTCTCGAACTCCTGGCCTCAGGTGATCCGCCTGTCTCGGCCTCCCAGAATGCTGG
GATTATAGACGTGAGCCACCGCATCCGGACTTTCCTTTTATGTAATAGTGATAATTCTATCCAAAGCATTTTTT
TTTTTTTTTGAGTCGGAGTCTCATTCTGTCACCCAGGCTGGAGGGTGGTGGCGCGATCTCGGCTTACTGCAA
CCTCTGCCTCCCGGGTTCAAGCGATTCTCCTGCCTCAGCCTCCTGAGTAGCTGGAATTACACACGTGCGCCA
CCATGGCCAGCTAATTTTTGTATTTTTAGTAGAGACGGGGTGTCACCATTTTGGCCAAGCTGGCCTCGAACTC
CTGACCTCAGGTGATCTGCCCGCCTCGGCTTCCCAAAGTGCTGGGATTACAGGTGTGAGCCACCGCGTCCT
GCTCCAAAGCATTTTCTTTCTATGCCTCAAAACAAGATTGCAAGCCAGTCCTCAAAGCGGATAATTCAAGAGC
TAACAGGTATTAGCTTAGGATGTGTGGCACTGTTCTTAAGGCTTATATGTATTAATACATCATTTAAACTCACA
ACAACCCCTATAAAGCAGGGGGCACTCATATTCCCTTCCCCCTTTATAATTACGAAAAATGCAAGGTATTTTC
AGTAGGAAAGAGAAATGTGAGAAGTGTGAAGGAGACAGGACAGTATTTGAAGCTGGTCTTTGGATCACTGTG
CAACTCTGCTTCTAGAACACTGAGCACTTTTTCTGGTCTAGGAATTATGACTTTGAGAATGGAGTCCGTCCTT
CCAATGACTCCCTCCCCATTTTCCTATCTGCCTACAGGCAGAATTCTCCCCCGTCCGTATTAAATAAACCTCA
TCTTTTCAGAGTCTGCTCTTATACCAGGCAATGTACACGTCTGAGAAACCCTTGCCCCAGACAGCCGTTTTAC
ACGCAGGAGGGGAAGGGGAGGGGAAGGAGAGAGCAGTCCGACTCTCCAAAAGGAATCCTTTGAACTAGGG
TTTCTGACTTAGTGAACCCCGCGCTCCTGAAAATCAAGGGTTGAGGGGGTAGGGGGACACTTTCTAGTCGTA
CAGGTGATTTCGATTCTCGGTGGGGCTCTCACAACTAGGAAAGAATAGTTTTGCTTTTTCTTATGATTAAAAGA
AGAAGCCATACTTTCCCTATGACACCAAACACCCCGATTCAATTTGGCAGTTAGGAAGGTTGTATCGCGGAG
GAAGGAAACGGGGCGGGGGCGGATTTCTTTTTAACAGAGTGAACGCACTCAAACACGCCTTTGCTGGCAGG
CGGGGGAGCGCGGCTGGGAGCAGGGAGGCCGGAGGGCGGTGTGGGGGGCAGGTGGGGAGGAGCCCAGT
CCTCCTTCCTTGCCAACGCTGGCTCTGGCGAGGGCTGCTTCCGGCTGGTGCCCCCGGGGGAGACCCAACC
TGGGGCGACTTCAGGGGTGCCACATTCGCTAAGTGCTCGGAGTTAATAGCACCTCCTCCGAGCACTCGCTC
ACGGCGTCCCCTTGCCTGGAAAGATACCGCGGTCCCTCCAGAGGATTTGAGGGACAGGGTCGGAGGGGGC
TCTTCCGCCAGCACCGGAGGAAGAAAGAGGAGGGGCTGGCTGGTCACCAGAGGGTGGGGCGGACCGCGT
GCGCTCGGCGGCTGCGGAGAGGGGGAGAGCAGGCAGCGGGCGGCGGGGAGCAGCATGGAGCCGGCGGC
GGGGAGCAGCATGGAGCCTTCGGCTGACTGGCTGGCCACGGCCGCGGCCCGGGGTCGGGTAGAGGAGGT
GCGGGCGCTGCTGGAGGCGGGGGCGCTGCCCAACGCACCGAATAGTTACGGTCGGAGGCCGATCCAGGT
GGGTAGAGGGTCTGCAGCGGGAGCAGGGGATGGCGGGCGACTCTGGAGGACGAAGTTTGCAGGGGAATT
GGAATCAGGTAGCGCTTCGATTCTCCGGAAAAAGGGGAGGCTTCCTGGGGAGTTTTCAGAAGGGGTTTGTA
ATCACAGACCTCCTCCTGGCGACGCCCTGGGGGCTTGGGAAGCCAAGGAAGAGGAATGAGGAGCCACGCG
CGTACAGATCTCTCGAATGCTGAGAAGATCTGAAGGGGGGAACATATTTGTATTAGATGGAAGTATGCTCTTT
ATCAGATACAAAATTTACGAACGTTTGGGATAAAAAGGGAGTCTTAAAGAAATGTAAGATGTGCTGGGACTAC
TTAGCCTCCAATTCACAGATACCTGGATGGAGCTTATCTTTCTTACTAGGAGGGATTATCAGTGGAAATCTGT

FIG. 27A

GGTGTATGTTGGAATAAATATCGAATATAAATTTTGATCGAAATTATTCAGAAGCGGCCGGGCGCGGTGCCTC
ACGCCTTGTAATCCCTTCACTTTGGGAGATCAAGGCGGGGGGAATCACCTGAGGTCGGGAGTTCGAGACCA
GCCTGGCCAACAGGTGAAACCTCGCCTCTACTAAAAATACAAAAAGTAGCCGGGGGTGGTGGCAGGCGCCT
GTAATCCCAGCTACTCGGGAGGTTGAGGCAGGAGAATCGCTTGAACCCGGGAGGCTGAGGTTGTAGTGAAC
AGCGAGATGGAGCCACTTCACTCCAGCCTGGGTGACAGAGTGAGACTTTGTCGAAAGAAAGAAAGAGAGAA
AGAGAGAGAGAAAAATTATTCAGAAGCAACTACATATTGTGTTTATTTTTAACTGAGTAGGGCAAATAAATATA
TGTTTGCTGTAGGAACTTAGGAAATAATGAGCCACATTCATGTGATCATTCCAGAGGTAATATGTAGTTACCAT
TTTGGGAATATCTGCTAACATTTTTGCTCTTTTACTATCTTTAGCTTACTTGATATAGTTTATTTGTGATAAGAG
TTTTCAATTCCTCATTTTTGAACAGAGGTGTTTCTCCTCTCCCTACTCCTGTTTTGTGAGGGAGTTAGGGGAG
GATTTAAAAGTAATTAATACATGGGTAACTTAGCATCTCTAAAATTTTGCCAACAGCTTGAACCCGGGAGTTTG
GCTTTGTAGTCCTACAATATCTTAGAAGAGACCTTATTTGTTTAAAAACAAAAAGGAAAAAGAAAAGTGGATAG
TTTTGACAATTTTTAATGGAG

FIG. 27B

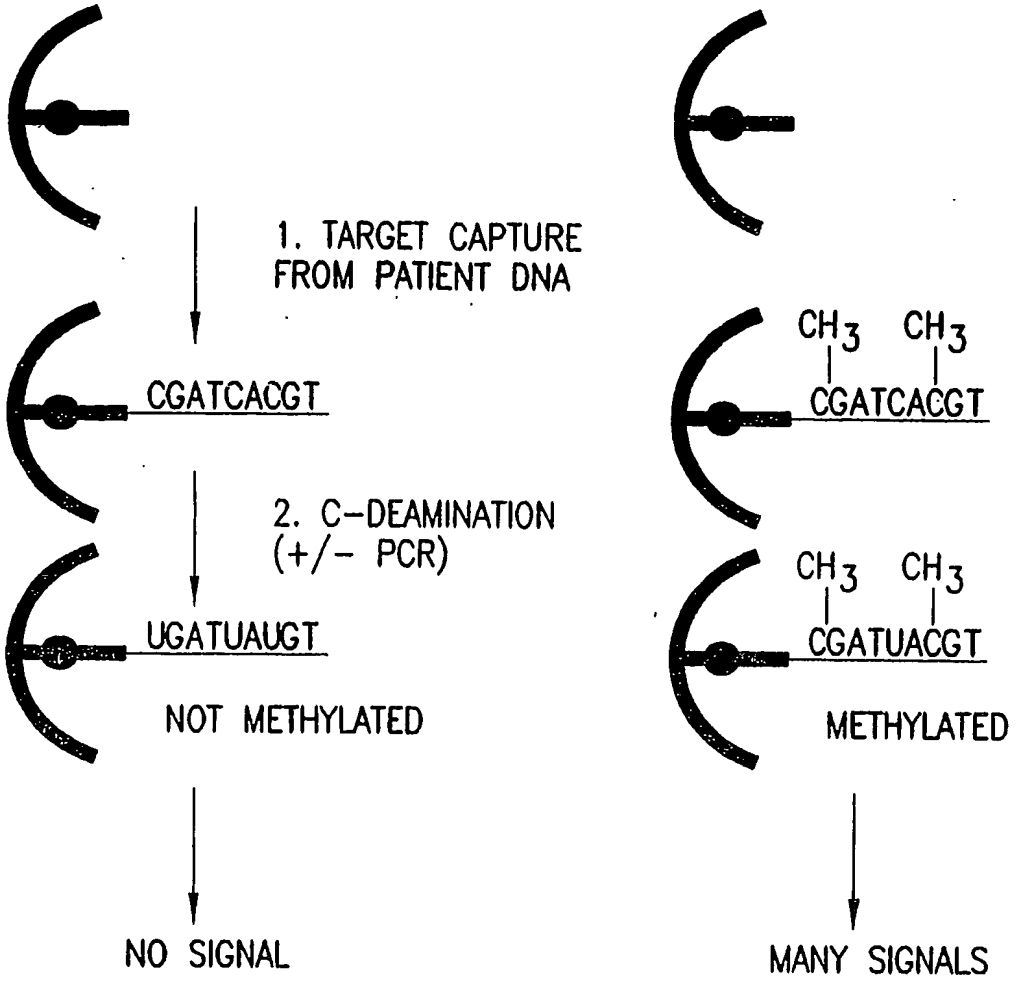

1. TARGET CAPTURE
FROM PATIENT DNA
CGATCACGT
2. C-DEAMINATION
(+/- PCR)
UGATUAUGT
NOT METHYLATED
NO SIGNAL
CH3 CH3
CGATCACGT
CH3 CH3
CGATUACGT
METHYLATED
MANY SIGNALS

FIG. 28

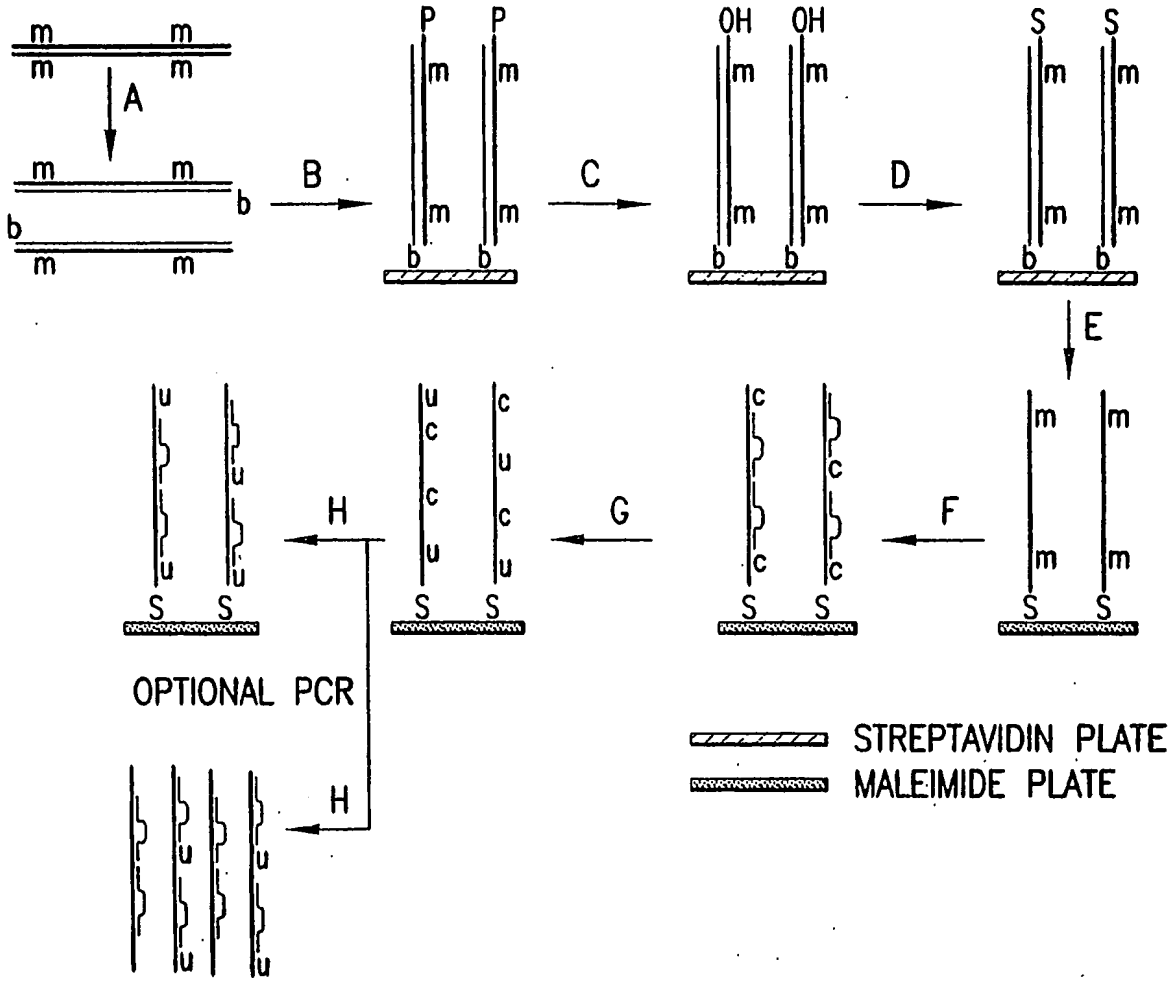

A
B
C
D
E
F
G
H
H
OPTIONAL PCR
STREPTAVIDIN PLATE
MALEIMIDE PLATE

FIG. 29

poly[dG-dC]

...GCGCGCGCGCGC...

FIG. 30A

Bubble complex 1

```
                          +1
                          |
                    TATATTTAGCCC
5' GGATACTTACAGCCAT              TACTCCATTCCATCCCGGGTTCGTCC Non-template
strand
3' CCTATGAATGTCGGTACCTGTGCCGCTTATGAGGTAAGGTAGGGCCCAAGCAGG Template strand
                          AA incorporate UTP
                           AU incorporate ATP
```

FIG. 30B

Template strand

3' CCTATGAATGTCGGTACCTGTGCCGCTTATGAGGTAAGGTAGGGCCCAAGCAGG

FIG. 30C

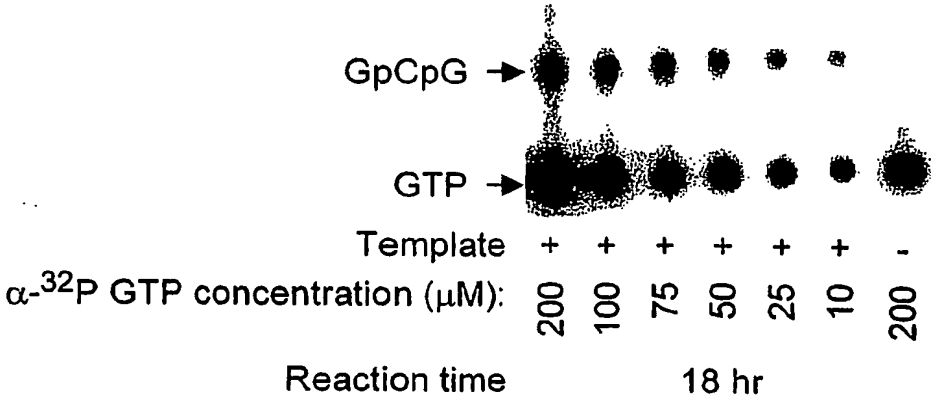


FIG. 31A

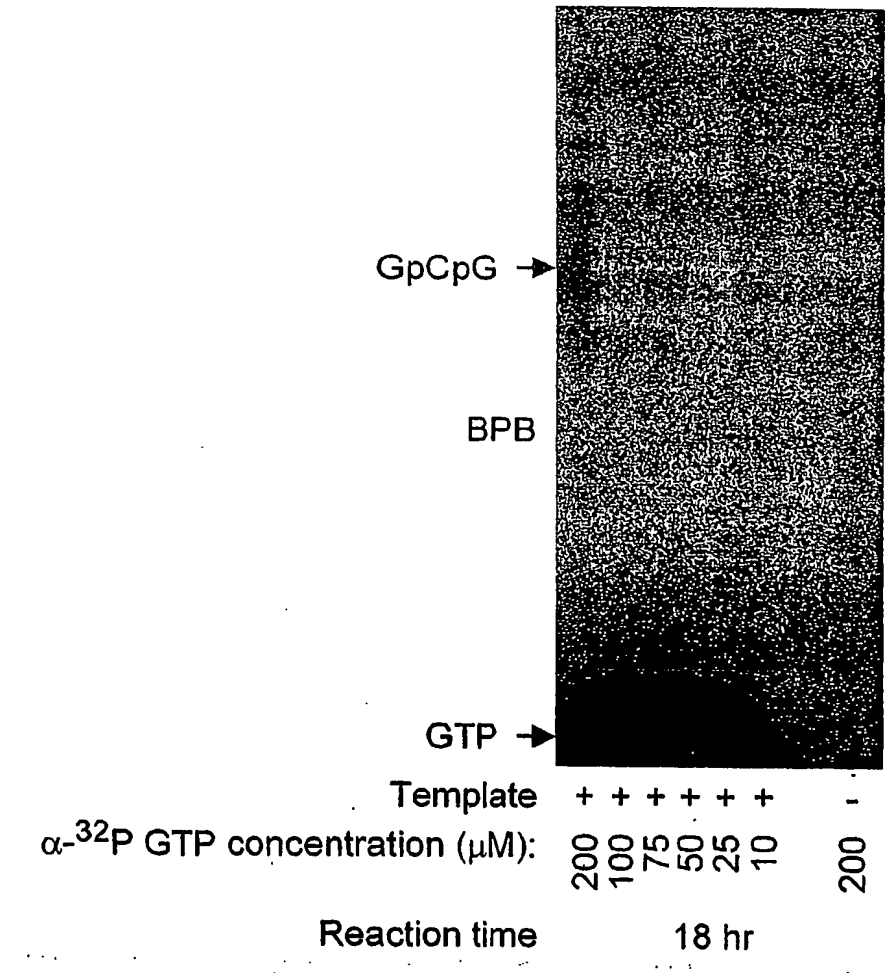
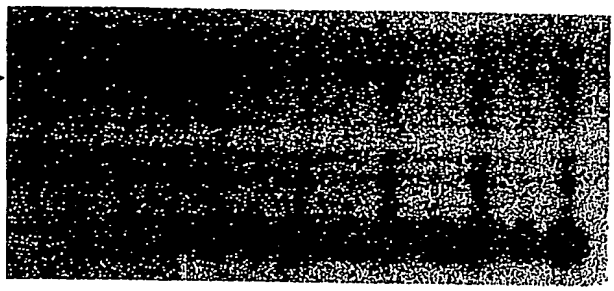
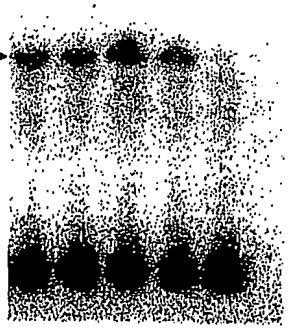


FIG. 31B



Sample	1	2	3	4	5	6	7	8	9	10	11	12
Bubble complex	+	+	+	+								
Template strand					+	+	+	+				
ApA	+	-	+	-	+	-	+	-	+	-	+	-
ApU	-	+	-	+	-	+	-	+	-	+	-	+
0 M Na acetate	+	+	-	-	+	+	-	-	+	+	-	-
0.15 M Na acetate	-	-	+	+	-	-	+	+	-	-	+	+
Reaction time	18 hr											

FIG. 32



E. coli holoenzyme	+	UTP
E. Coli Core	+	
T7 RNA pol	+	
SP6 RNA pol	+	

FIG. 33

FIG. 34A

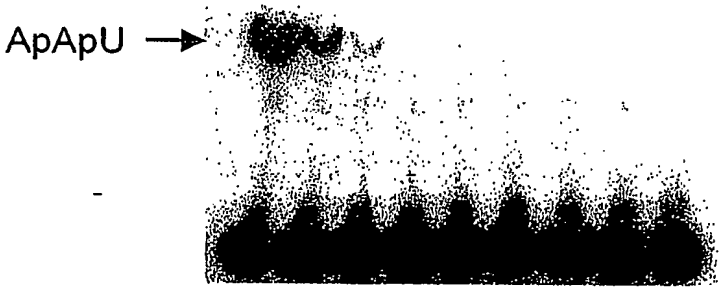


FIG. 34B

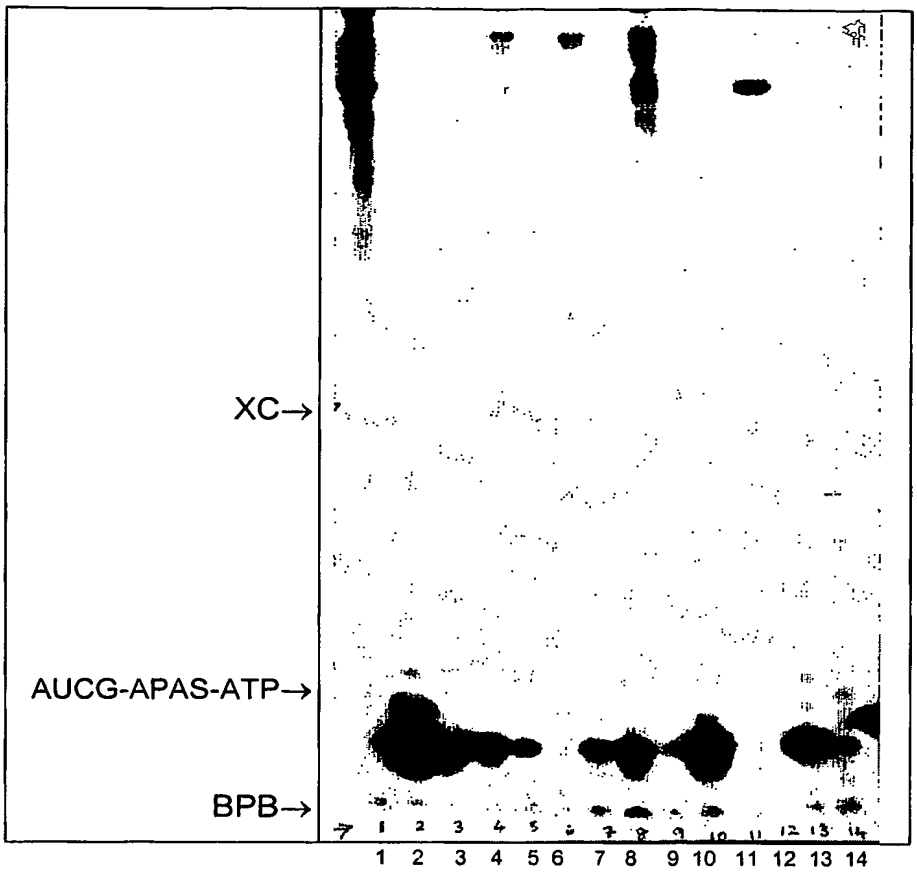
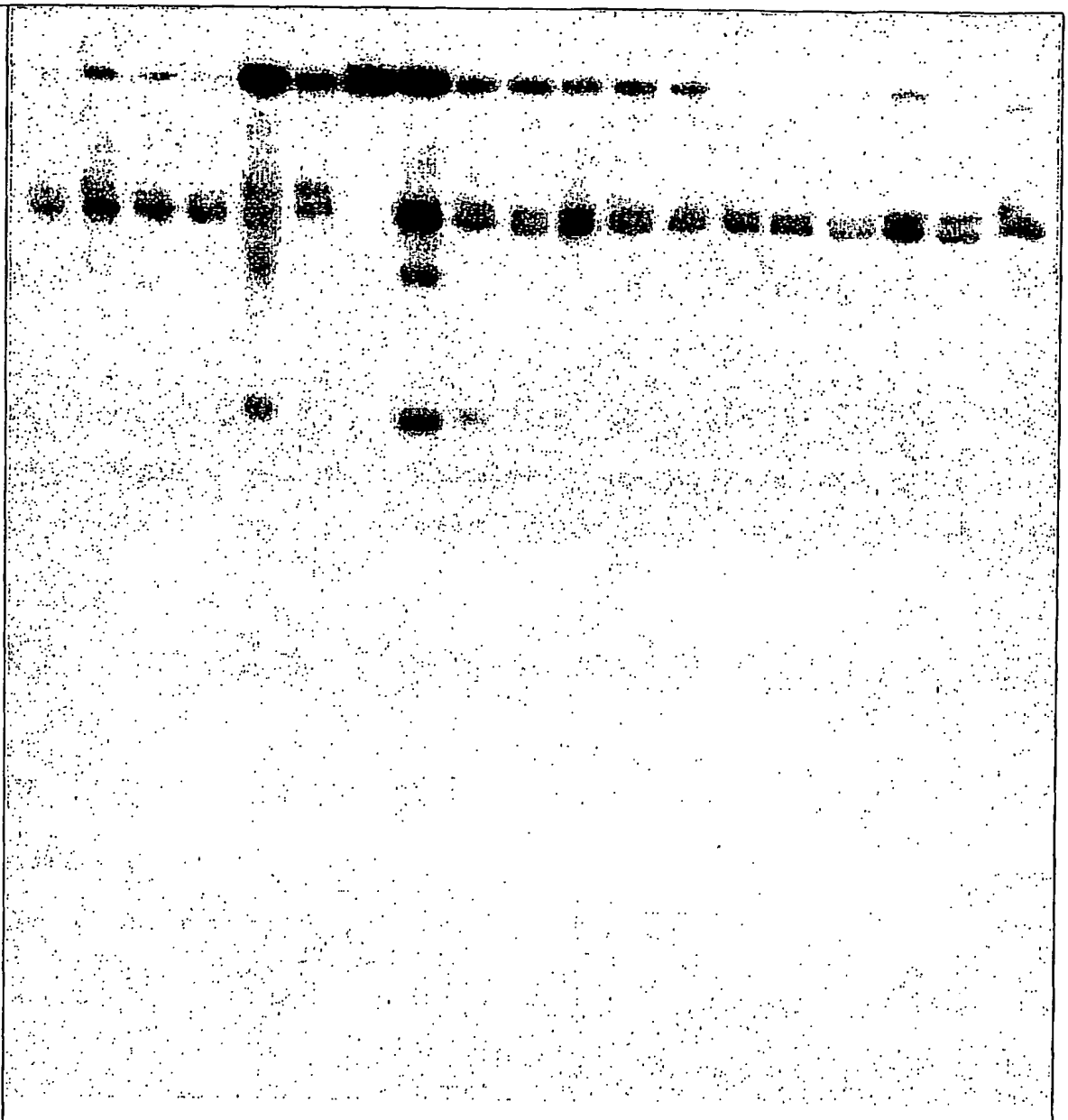


FIG. 35

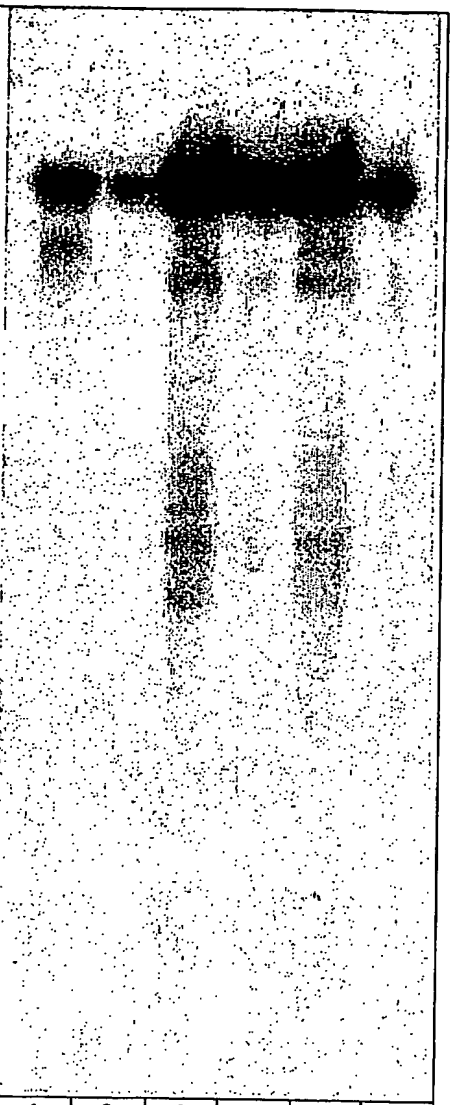
FIG. 36



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Sequenase	+	+	+	+															
Therminator					+	+	+												
Vent exo-								+	+	+									
Klenow exo-											+	+	+						
AMV RT														+	+	+			
M-MLV RT																	+	+	+
SH-dUTP %	0	0	90	100	0	90	100	0	90	100	0	90	100	0	90	100	0	90	100
DdTTP	+																		

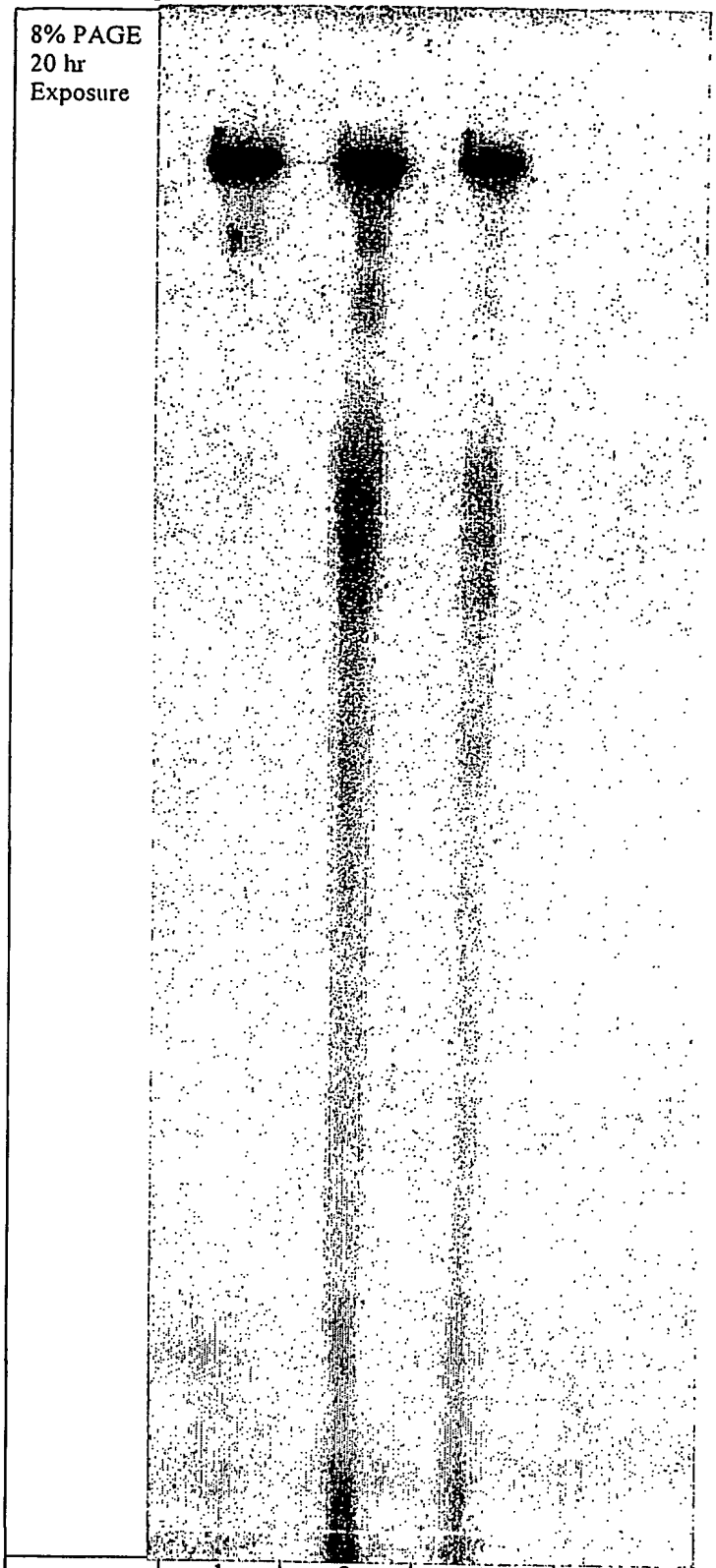
FIG. 37

8% PAGE
16 hr Exposure



	1	2	3	4	5	6
SH-dUTP	+	+	-	-	-	-
DTTP	-	-	+	+	-	-
ddTTP	-	-	-	-	+	+
µL of Reaction	20	5	20	5	20	5

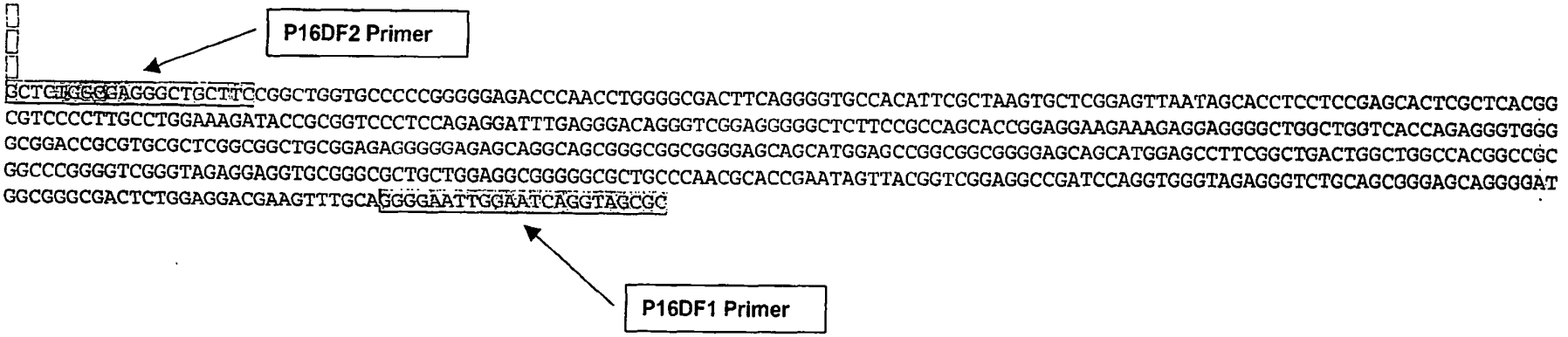
FIG. 38



	1	2	3	4
SH-Dutp	+	–	–	
DTTP	–	+	–	
DdTTP	–	–	+	
DNA	+	+	+	–

FIG. 39

P16DF PCR



1st T after P16DF2 = 24mer
1st TT after P16DF2 = 60mer
1st TTT after P16DF2 = 169mer

FIG. 40A

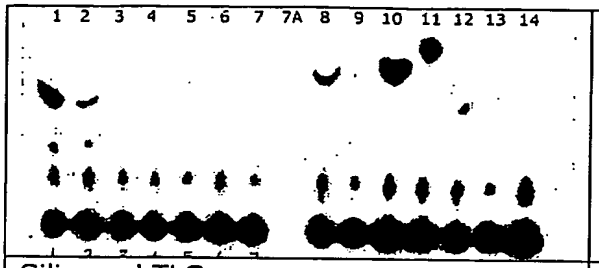
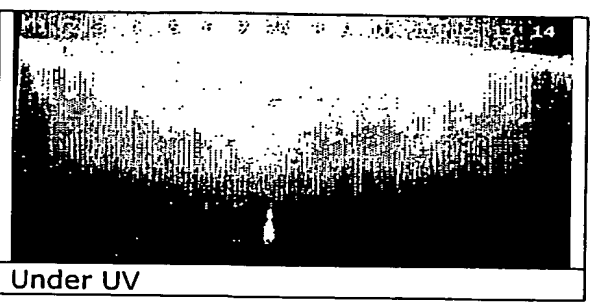


FIG. 40B



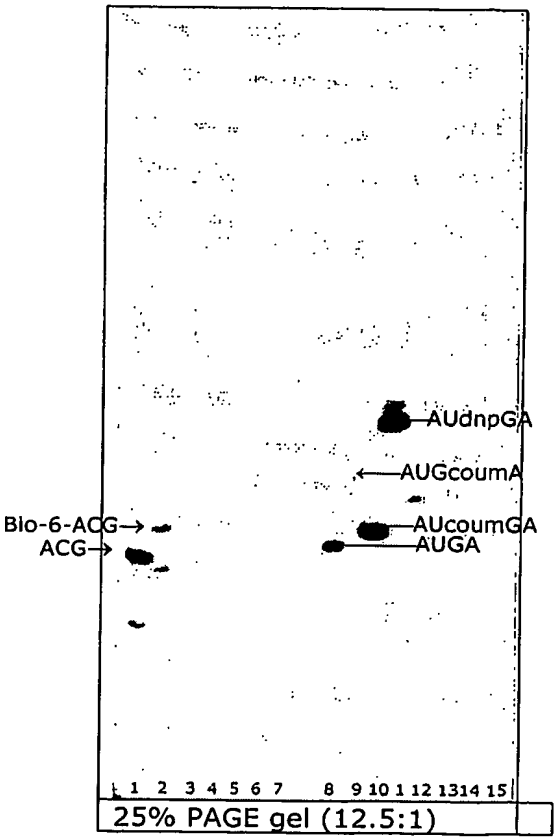
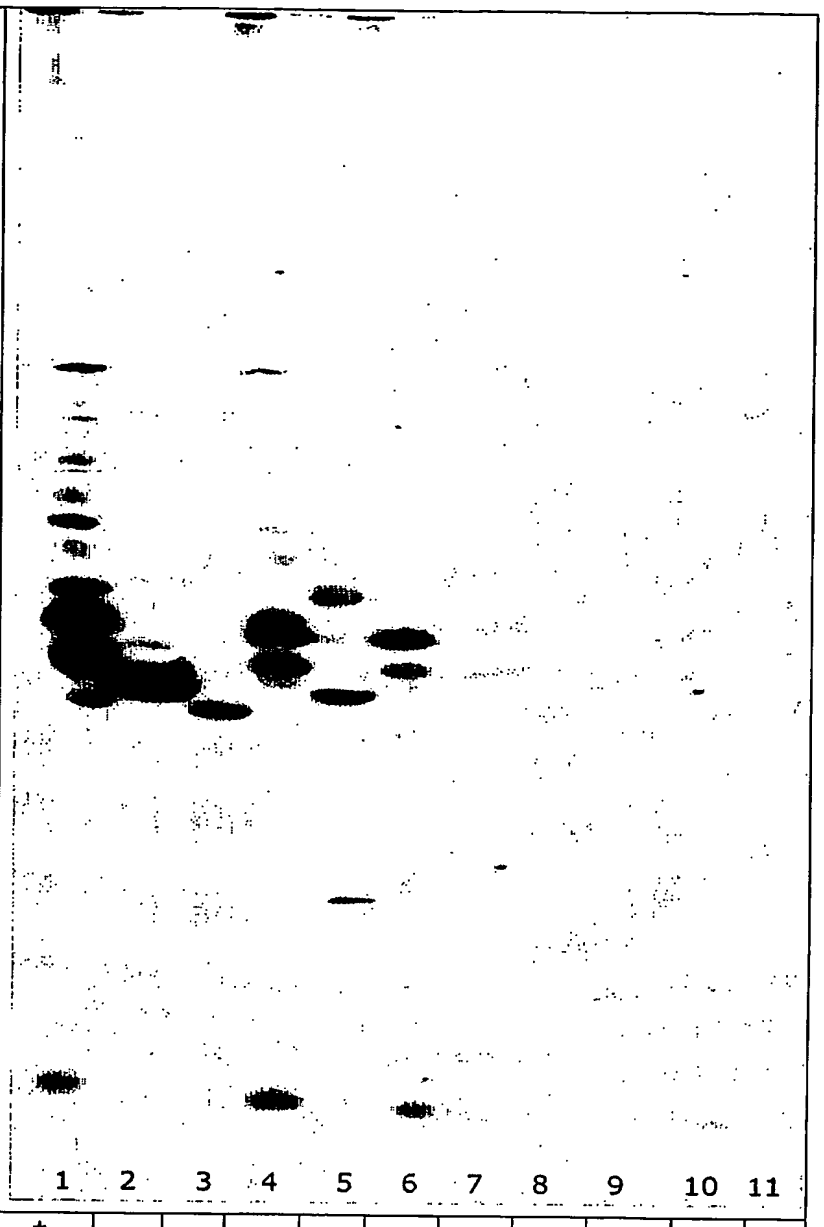


FIG. 40C



ApU+ C+G	+										
ApU+ C		+									
ApU+couG+3'OmeA			+								
PyApU+C+G				+							
PyApU+C					+						
PyApU+C+couG						+					
PyApU+C+couA							+				
PyApU+couG+3'OmeA								+			
α^{32}P-GTP		+			+		+		+		
α^{32}P-ATP	+			+		+				+	
α^{32}P-CTP			+					+			+

FIG. 41A

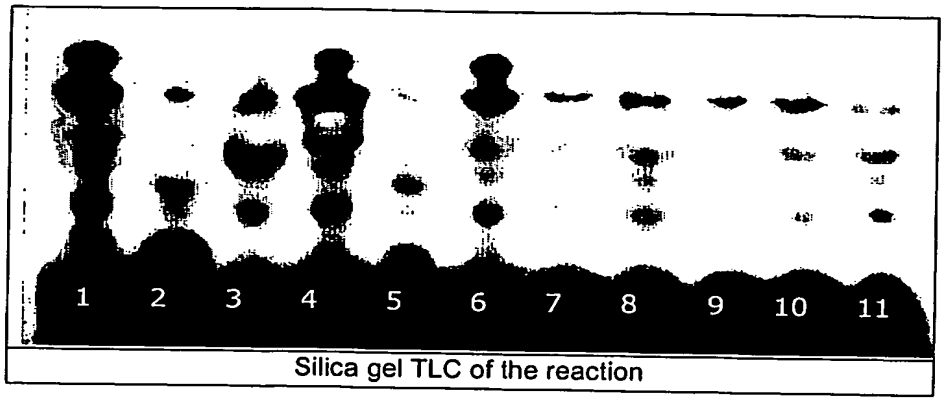
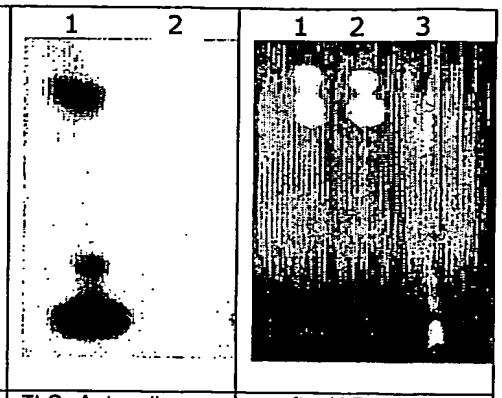


FIG. 41B



	TLC, Autoradiogram		after IAF, UV		
AU-HIP/S10	+	+	+	+	
UpA	+	+	+	+	
Bis-CTP	+	+	+	+	
TCEP	+	+	+	+	
α-^{32}P UTP	+		+		
5-IAF			+	+	
SF-CTP					+

FIG. 42

FIG. 43

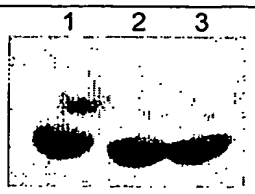
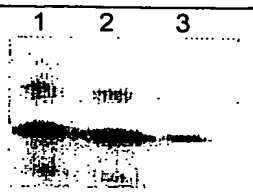
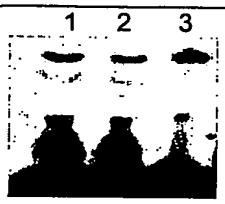
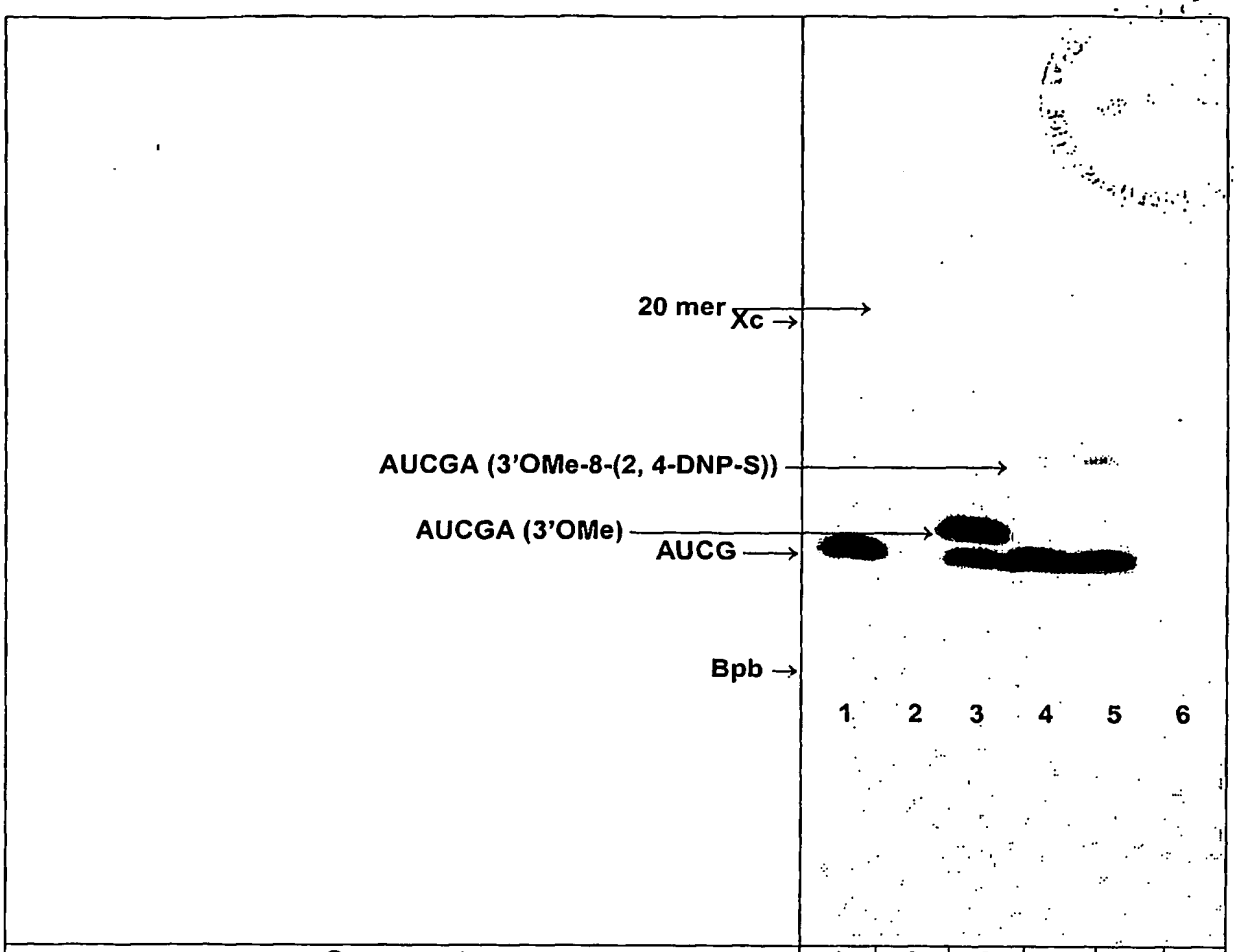
	A. 8%polyacrylamide/ 7M urea gel	B.25%polyacrylamide /7M urea gel	C. Silica gel
20 mer →			

FIG. 44



Components					1	2	3	4	5	6
ApU	CTP	α^{32}P-GTP			+					
ApU	CTP	α^{32}P-GTP	ATP			+				
ApU	CTP	α^{32}P-GTP		3'OMe-ATP			+			
ApU	CTP	α^{32}P-GTP		3'OMe-8-(2, 4-DNP-S)-ATP				+		
ApU	CTP	α^{32}P-GTP		3'OMe-8-(2, 4-DNP-S)-ATP					+	
		α^{32}P-GTP								+

SEQUENCE LISTING

<110> Ribomed Biotechnologies, Inc.
Hanna, Michelle M.

<120> Molecular Detection Systems Utilizing Reiterative Oligonucleotide Synthesis

<130> 2072.001PC05

<150> US 10/425,037
<151> 2003-04-29

<150> PCT/US02/34419
<151> 2002-10-29

<150> US 09/984,664
<151> 2001-10-30

<160> 3

<170> PatentIn version 3.2

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<213> Artificial

<220>
<223> P16DF2 Primer

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<210> 2
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<213> Artificial

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acggcgtccc cttgcctgga aagataccgc ggtccctcca gaggatttga gggacagggt 180

cggaggggge tcttccgcca gcaccggagg aagaaagagg aggggctggc tggtcaccag 240

agggtggggc ggaccgcgtg cgctcggcgg ctgcggagag ggggagagca ggcagcgggc 300

ggcggggagc agcatggagc cggcggcggg gagcagcatg gagccttcgg ctgactggct 360

ggccacggcc gcggcccggg gtcgggtaga ggaggtgcgg gcgctgctgg aggcgggggc 420

gctgcccaac gcaccgaata gttacggtcg gaggccgatc caggtgggta gagggtctgc 480

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aggtagcgc 549